U.S. DEPARTMENT OF COMMERCE
National Technical Information Service

PB-256 735

Air Pollution Assessment of Toluene

Mitre Corporation

Prepared For
Environmental Protection Agency

May 1976

BEST SELLERS

FROM
NATIONAL
TECHNICAL
INFORMATION
SERVICE

Comparison of Energy Consumption Between West Germany and the United States
PB-245 652/ PAT 112 p. PC$5.50/MF$3.00

A Comprehensive Policy to Ameliorate Adverse Impacts of Transportation Facilities
PB-247 823/ PAT 138 p. PC$6.00/MF$3.00

A Comprehensive Policy to Ameliorate Adverse Impacts of Transporation Facilities, Appendix
PB-247 824/ PAT 310 p. PC$9.75/MF$3.00

Demand for Coal for Electricity Generation 1975–1984
PB-245 216/ PAT 40 p. PC$4.00/MF$3.00

A National Study of Adolescent Drinking Behavior, Attitudes and Correlates
PB-246 002/ PAT 405 p. PC$11.00/MF$3.00

Energy from Coal: Guidelines for the Preparation of Environmental Impact Statements
PB-242 960/ PAT 258 p. PC$9.00/MF$3.00

Energy Versus the Environment: The Issues
PB-246 382/ PAT 35 p. PC$4.00/MF$3.00

Improving the Dissemination of Scientific and Technical Information: A Practitioner's Guide to Innovation
PB-247 057/ PAT 203 p. PC$7.75/MF$3.00

Investigation and Evaluation of Cracking in Austenitic Stainless Steel Piping of Boiling Water Reactor Plants
PB-246 645/ PAT 123 p. PC$5.50/MF$3.00

Pipeline Industry's Practices Using Plastic Pipe in Gas Pipeline Facilities and the Resulting Safety Factors
PB 247 301/ PAT 436 p. PC$11.75/MF$3.00

NOx Combustion Control Methods and Costs for Stationary Sources. Summary Study.
PB-246 750/ PAT 117 p. PC$5.50/MF$3.00

Reactor Safety Study: An Assessment of Accident Risks in U.S. Commercial Nuclear Power Plants
PB-248 200/SET/ PAT 2,504 p. 8 Volumes PC$61.00

Report on Sulfur Oxide Control Technology
PB-248 667/ PAT 89 p. PC$5.00/MF$3.00

Research Evaluation of a System of Natural Air Conditioning
PB-243 498/ PAT 384 p. PC$10.50/MF$3.00

Retrofitting a Residence for Solar Heating and Cooling: The Design and Construction of the System
PB-247 482/ PAT 101 p. PC$5.50/MF$3.00

Saudi Arabia Five-Year Plan, 1975–1980
PB-246 572/ PAT 683 p. PC$16.25/MF$3.00

Shotcrete Practice in Underground Construction
PB-248 765/ PAT 501 p. PC$12.75/MF$3.00

Short-Term Coal Forecast, 1975–1980
PB-247 073/ PAT 120 p. PC$5.50/MF$3.00

State Energy Information Systems: A Survey
PB-247 457/ PAT 84 p. PC$4.50/MF$3.00

A Study of Fixed Capital Requirements of the U.S. Business Economy
PB-248 690/ PAT 84 p. PC$5.00/MF$3.00

Sulfates and the Environment—A Review
PB-248 122/ PAT 155 p. PC$6.75/MF$3.00

HOW TO ORDER

When you indicate the method of payment, please note if a purchase order is not accompanied by payment, you will be billed an addition $5.00 *ship and bill* charge. And please include the card expiration date when using American Express.

Normal delivery time takes three to five weeks. It is vital that you order by number or your order will be manually filled, insuring a delay. You can opt for *airmail delivery* for a $2.00 charge per item. Just check the *Airmail Service* box. If you're really pressed for time, call the NTIS Rush Order Service. (703) 557-4700. For a $10.00 charge per item, your order will be airmailed within 48 hours. Or, you can pick up your order in the Washington Information Center & Bookstore or at our Springfield Operations Center within 24 hours for a $6.00 per item charge.

You may also place your order by telephone or TELEX. The order desk number is (703) 557-4650 and the TELEX number is 89-9405.

Whenever a foreign sales price is NOT specified in the listings, all foreign buyers must add the following charges to each order: $2.50 for each paper copy; $1.50 for each microfiche; and $10.00 for each Published Search.

Thank you for your interest in NTIS. We appreciate your order.

METHOD OF PAYMENT

☐ Charge my NTIS deposit account no._____

☐ Purchase order no._____

☐ Check enclosed for $_____

☐ Charge to my American Express Card account number

Card expiration date_____

Signature_____

☐ Airmail Services requested

NAME_____

ADDRESS_____

CITY, STATE, ZIP_____

Item Number	Quantity		Unit Price*	Total Price*
	Paper Copy (PC)	Microfiche (MF)		
			Sub Total	
			Additional Charge	
			Enter Grand Total	

All Prices Subject to Change
8/76

Clip and mail to:

NTIS

National Technical Information Service
U.S. DEPARTMENT OF COMMERCE
Springfield, Va. 22161
(703) 557-4650 TELEX 89-9405

PB 256 735

Air Pollution Assessment of Taiwan

P. WISER

MAY 1976

REPRODUCED BY
NATIONAL TECHNICAL
INFORMATION SERVICE
U. S. DEPARTMENT OF COMMERCE
SPRINGFIELD, VA. 22161

MITRE
METEK

TECHNICAL REPORT DATA
(Please read Instructions on the reverse before completing)

1. REPORT NO.	2.	3. RECIPIENT'S ACCESSION NO.
MTR-7215		

4. TITLE AND SUBTITLE	5. REPORT DATE
Air Pollution Assessment of Toluene	May 1976
	6. PERFORMING ORGANIZATION CODE

7. AUTHOR(S)	8. PERFORMING ORGANIZATION REPORT NO.
P. Walker	

9. PERFORMING ORGANIZATION NAME AND ADDRESS	10. PROGRAM ELEMENT NO.
The Mitre Corporation McLean, Virginia 22101	11. CONTRACT/GRANT NO. 68-02-1495

12. SPONSORING AGENCY NAME AND ADDRESS	13. TYPE OF REPORT AND PERIOD COVERED
U. S. Environmental Protection Agency Office of Air and Waste Management Office of Air Quality Planning and Standards Research Triangle Park, North Carolina 27711	Final
	14. SPONSORING AGENCY CODE EPA-AWM

15. SUPPLEMENTARY NOTES

16. ABSTRACT

Toluene, a homolog of benzene, is primarily a central nervous system depressant in both humans and animals. Only inconclusive evidence for hematopoietic or myelotoxic dysfunction was found. Toluene is produced in the U. S. from both coal and petroleum; however, the majority of this production is petroleum derived. Exposure of the human population to toluene can ensue not only from production facility emissions, but also from gasoline evaporation or automobile and coke oven emissions. The average concentration of toluene in urban air is reportedly 0.01 to 0.05 ppm. Control technology has been developed which, if utilized, can provide protection to industrial workers.

17. KEY WORDS AND DOCUMENT ANALYSIS

a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group
Organic Compounds Hydrocarbons Organic Solvents Physiological Effects Air Pollution Control Stationary Sources	Air Pollution Automobiles	

PRICES SUBJECT TO CHANGE

18. DISTRIBUTION STATEMENT	19. SECURITY CLASS (This Report)	21. NO. OF PAGES
Unlimited	Unclassified	101
	20. SECURITY CLASS (This page)	22. PRICE
	Unclassified	$5.50

EPA Form 2220-1 (9-73)

CONTROLLED DISTR.

MITRE Technical Report
MTR-7215

Air Pollution Assessment of Toluene

P. WALKER

MAY 1976

CONTRACT SPONSOR	U.S. Environmental Protection Agency
CONTRACT NO.	68-02-1495
PROJECT NO.	0778
DEPT.	W-54

THE MITRE
McLEAN, VIRGINIA 22101

Department Approval: _____

Jack Golden

MITRE Project Approval: _____

Lydia W. Thomas

ABSTRACT

Toluene, a homolog of benzene, is primarily a central nervous system depressant in both humans and animals. Only inconclusive evidence for hematopoietic or myelotoxic dysfunction was found. Toluene is produced in the U.S. from both coal and petroleum; however, the majority of this production is petroleum derived. Exposure of the human population to toluene can ensue not only from production facility emissions, but also from gasoline evaporation or automobile and coke oven emissions. The average concentration of toluene in urban air is reportedly 0.01 to 0.05 ppm. Control technology has been developed which, if utilized, can provide protection to industrial workers.

ACKNOWLEDGMENT

The author wishes to recognize those individuals who generously offered assistance and time during the compilation of this document (one month time period). Included are Mike Jones, Richard Johnson, and Justice Manning of the U.S. Environmental Protection Agency, and Linda Duncan, Edward Preston, Dr. Bernard Baratz, Dr. Robert Ouellette, and Dr. Lydia Thomas of The MITRE Corporation.

TABLE OF CONTENTS

	Page
I. SUMMARY, CONCLUSIONS AND RECOMMENDATIONS	1
A. PHYSICAL AND CHEMICAL PROPERTIES	1
B. EFFECTS	1
C. AMBIENT DATA	4
D. POPULATION AT RISK	5
E. MEASUREMENT TECHNOLOGY	6
F. SOURCES	6
G. CONTROL	8
II. AIR POLLUTION ASSESSMENT REPORT	10
A. PHYSICAL AND CHEMICAL PROPERTIES	10
B. EFFECTS	23
1. Humans	23
2. Animals	35
3. Other Effects	41
C. AMBIENT DATA, POPULATION AT RISK AND MEASUREMENT TECHNOLOGY	46
D. SOURCES	55
E. CONTROL	77
REFERENCES	81

TABLE OF CONTENTS (CONTINUED)

LIST OF TABLES

TABLE NUMBER		Page
I	PHYSICAL PROPERTIES OF TOLUENE	11
II	AZEOTROPES OF TOLUENE	16
III	RELATIVE RATES OF SUBSTITUTION IN BENZENE AND TOLUENE	17
IV	EFFECTS OF TOLUENE EXPOSURE ON HUMANS AND ANIMALS	30
V	REPORTED TOLUENE TOXICITY TO AQUATIC ANIMALS	44
VI	TOLUENE PRODUCTION BY DERIVATIVE (1971)	56
VII	U.S. TOLUENE PRODUCTION CAPACITY (1975)	57
VIII	TOLUENE CONTENT OF PYROLYSIS GASOLINE	61
IX	CONSUMPTION OF TOLUENE	69
X	UPPER LIMIT OF THE AMOUNT OF TOLUENE LOST FROM BY-PRODUCT MANUFACTURING FACILITIES IN 1971	70
XI	LOCATION AND TOLUENE USAGE CAPACITY OF FACILITIES PRODUCING BENZOIC ACID AND TOLUENE DIISOCYANATE FROM TOLUENE (1972)	71
XII	TOLUENE EMISSIONS TO THE ENVIRONMENT	76

LIST OF FIGURES

FIGURE NUMBER		
1	THE STRUCTURAL FORMULA FOR TOLUENE	14
2	GEOGRAPHIC DISTRIBUTION AND RELATIVE CAPACITIES OF TOLUENE PRODUCTION FACILITIES	58

TABLE OF CONTENTS (CONCLUDED)

LIST OF FIGURES (CONCLUDED)

FIGURE NUMBER		Page
3	DISTRIBUTION AND RELATIVE CAPACITIES OF TOLUENE PRODUCTION FACILITIES ON THE TEXAS AND LOUISIANA COASTS	59
4	COMMERCIAL USES OF TOLUENE AND TOLUENE DERIVATIVES	65
5	THE FLOW OF TOLUENE THROUGH THE UNITED STATES IN 1971	67

AIR POLLUTION ASSESSMENT OF TOLUENE

I. SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

A. PHYSICAL AND CHEMICAL PROPERTIES

Toluene is a homolog of benzene in which one hydrogen atom has been replaced by a methyl radical. It is quite stable in air, slightly soluble in water, and miscible in alcohol, ether, and benzene. Exposure to toluene, whether in industrial situations or in the general environment, can either be to the relatively pure, reagent grade toluene or to industrial grade toluene containing up to 25 percent benzene. Exposure can also ensue from gasoline evaporation or automobile and coke oven emissions. As late as the 1940's, reagent grade toluene was not readily obtainable in the United States, while it was mid-1950 before pure toluene was available world-wide. The purity of toluene must be established in toxicity evaluations or the symptomatic effects of benzene exposure will mask or magnify the toxic effects of toluene. This contamination renders the majority of the pre-1940's United States observations invalid unless purity is specifically noted. For the rest of the world, much of the pre-1950's experimental data should be eliminated with some of the data reported after the 1950's doubtful due to questionable toluene composition.

B. EFFECTS

Inhalation of toluene rapidly results in the equilibration of the blood with the ambient toluene concentration, due to the low

solubility of the hydrocarbon in the blood. Toluene is quite lipophilic, however, and accumulates readily in the lipoid-containing organs. Metabolism occurs primarily by oxidation of the methyl radical, yielding benzoic acid which is rendered water soluble by conjugation with glycine and finally eliminated as hippuric acid. An additional metabolic pathway available in rats was substantiated by the detection of an increase in organic sulfate in the excreta. The necessity of this alternate metabolic method in rats may be explained by the poor excretion of toluene metabolites in the bile.

The liposolubility of toluene accounts for the primary human physiological response after acute or chronic exposure, which is disturbance of the central nervous system. Manifestation of this depression may be fatigue, drowsiness, confusion, headache, impaired coordination, nausea, or, at high enough concentrations, anesthesia. Other symptoms have been reported, with the intensity and the duration of the response directly related to the concentration and/or duration of the exposure. Twice weekly human exposures of eight hours each for three months elicited the following responses: at 50 to 100 ppm, drowsiness with slight headache; 200 ppm induced muscular weakness, confusion, incoordination, headache and nausea; at 300 to 400 ppm, severe fatigue, confusion, muscular weakness, headache, incoordination, with prolonged aftereffects; 600 ppm produced effects similar to 300 to 400 ppm with a staggering gait after eight hours and residual nervousness; at 800 ppm extreme nausea,

confusion, severe fatigue, lack of self-control and incoordination were noted after three hours with moderate to severe insomnia, lasting several days, noted as an aftereffect. A case of toluene habituation was characterized by headache, brief memory loss, and "inappropriate" speech and resulted in permanent cerebral atrophy.

Alteration of serum glycoprotein production, incidence of hepatorenal damage and hematopoietic dysfunction have all been reported, but involved exposure to toluene of either questionable purity or known impurities. The blood abnormalities reported after exposure are so consistent with those induced by benzene poisoning that either benzene contamination of the toluene or exposure to benzene in some other form cannot be overruled. The myelotoxicity of toluene has been reported; however, this too is most likely attributable to benzene-contamination of the toluene. The recent evidence indicates that pure toluene is neither myelotoxic nor is it damaging to the hematopoietic system.

The primary effect of toluene on laboratory animals closely parallels the major effect observed in humans, disturbance of the central nervous system. The majority of the available literature indicates no hematopoietic damage due to pure toluene exposure. However, the myelotoxicity of toluene with accompanying neutropoiesis in rats has been recently reported after subcutaneous administration of 0.8 g/kg for 12 days. The importance of these findings could be significant with subsequent experimental repetition and

replication of results. At this time, it would be prudent to institute similar investigations using inhalation, which is a more likely mode of human exposure, rather than injection. The appearance of additional reports of damage and alteration to the hematopoietic system in animals further indicates a need for definitive experimentation using pure toluene. Although toluene does not appear to be permanently damaging to humans in low concentrations, until such time as data are available pertaining to the long-term low-level effects on humans, industry should attempt to avoid the exposure of its employees or the general population to ambient toluene by instituting strict safety procedures and increasing employee awareness of the problem. This data, necessary for exposure limit evaluation, can be made available only by executing complete, controlled inhalation experiments on animals and by epidemiologic studies with accurately measured exposure levels and durations in humans.

C. AMBIENT DATA

In response to complaints during 1974, the Occupational Safety and Health Administration (OSHA) analyzed 1867 industrial atmospheric samples for the presence of toluene. However, a summary of the test results from those samples is not readily available. The expected concentration of toluene in urban air is reported to be 0.01 to 0.05 ppm, although the hydrocarbon is not routinely monitored in the atmosphere.

Ambient measurement programs for toluene should be developed in those areas suspected to represent major emission sources. These areas should include not only those with atmospheric levels of toluene detectable in the vicinity of production and utilization facilities, but also localities having significant numbers of coking operations, including Pittsburgh, Pennsylvania, Chicago, Illinois, and Birmingham, Alabama. Studies of this nature would provide an expeditious means of deployment of existing control technology to the areas of greatest need.

D. POPULATION AT RISK

To assess the risk of atmospheric toluene presented to the general population during production, a hypothetical production facility was calculated to effect a concentration of 2.3 mg/m^3 (0.623 ppm) 500 meters downwind of the plant using a crude diffusion model. This ambient concentration is greater than the level of 1.5 mg/m^3 (0.395 ppm), which reportedly enhanced brain electropotential. The significance of this effect on the electropotential of the brain has not been established. It is only clear that it is a measurable effect produced by toluene exposure at this concentration. An individual would have to remain at this same location for more than 275 days in order to inhale an amount equal to a worker exposed to the acceptable time-weighted average proposed by the National Institute for Occupational Safety and Health (NIOSH), of 100 ppm during a 40 hour work week.

Until such time as data are available pertaining to the long-term low-level effects of toluene on humans and the major source of emission, conservative practices should be implemented. Industry should attempt to avoid the exposure of its employees or the general population to ambient toluene by instituting strict safety procedures and increasing employee awareness of the problem. The data necessary for exposure limit evaluation can be developed by executing complete, controlled inhalation experiments on animals and by further epidemiologic studies with accurately measured levels and duration in humans.

E. MEASUREMENT TECHNOLOGY

Measurement technology presently used in the determination of toluene includes a variety of methods. Sample collection procedures include absorption in scrubbers by nitrating solutions or organic solvents, adsorption on silica gel or activated charcoal, or collection in plastic bags. Analysis of these samples after collection can be accomplished by spectrophotometry, colorimetric indicator tubes, and gas chromatography. Adsorption on activated charcoal provides the greatest ease and efficiency of collection, while gas chromatography yields the most specific and sensitive means of detection.

F. SOURCES

Toluene is commercially produced in the United States from both coal and petroleum, with the majority of this production being

petroleum-derived. The natural formation of coal may be a non-synthetic source of toluene, but little information is available concerning this potential supply. At the beginning of 1975, U.S. production capacity for toluene totaled 1040.5 million gallons per year. However, the major stationary emission sources for toluene do not appear to be production facilities but those facilities wherein it is consumed as a synthetic intermediate.

In 1971, over 50 percent of the toluene consumed in the United States was blended into gasoline. Demand for toluene as a constituent of gasoline continues; however, other industries utilize the hydrocarbon primarily as a solvent or as a chemical intermediate. Some of these chemical intermediates include toluene diisocyanate, benzyl chloride, phenol, and benzoic acid. These products are used in the manufacture of polyurethane materials, plasticizers, and adhesives.

Two additional sources of potential toluene contamination not arising from either commercial production or use are oil spills and motor vehicle emissions. It is calculated that 143 to 156 million pounds of toluene are released annually into oceans and waterways from spills, while gasoline evaporation and consumption releases approximately 3350 million pounds to the environment. Another source of environmental toluene is coke ovens. A calculated 29.8 million pounds of toluene were released to the environment based upon the 1974 estimates of coke production.

Environmental transport of toluene from the point of emission has not been clearly defined. Due to its ability to solubilize in water, atmospheric toluene could be introduced to the water via rainfall, after which volatilization to the atmosphere could occur. Therefore, a continuous cycling between the air and water is likely to occur, indicating significant environmental mobility and possible dispersion and distribution ability. Due to the long-term stability of toluene, a cumulative effect may take place.

G. CONTROL

Adequate efficient and simple measurement technology has been developed which, if employed, can provide protection to industrial workers. Toluene emissions can be controlled by using a vapor condensation apparatus in the form of scrubbers and separators in the catalytic reforming process. Routine maintenance of these mechanical additions would help eliminate the risk of high ambient toluene concentrations. Proper ventilation of the areas in a facility that utilizes toluene and isolation of these areas from other work regions would further reduce the possibility of hazardous toluene concentrations accumulating. Proper handling and transport techniques, if emphasized, add to the safety of not only the industrial worker but the general population as well.

The substitution of another material for toluene or replacement of open-system equipment could be 100 percent effective in reducing the toluene atmospheric emissions at industrial sites. However,

careful consideration must be given to the health hazards, as well as the operational and economical acceptability of the substitutes.

The problem posed by oil spills is more ubiquitous and will probably be affected only by legislation imposing still penalties and/or fines on the involved companies (i.e., oil producers and transporters). The vehicle emission controls recently instituted are effectively reducing ambient nonmethane hydrocarbon levels from automobiles. Toluene levels from this source should also continue to decline as older noncontrolled cars are retired.

II. AIR POLLUTION ASSESSMENT REPORT

A. PHYSICAL AND CHEMICAL PROPERTIES

Toluene, also called toluol or methylbenzene, is a clear, colorless, refractive, noncorrosive liquid with a sweet pungent odor similar to that of benzene. It is highly flammable and burns with a luminous, sooty flame, leaving a carbon residue. Toluene is a homolog of benzene in which one hydrogen atom has been replaced by a methyl radical. This accounts for the physical and behavioral similarities of the two hydrocarbons (1, 2, 3).

Toluene is quite stable in air and only slightly soluble in water, 515 to 540 parts of toluene per million parts of water. The solubility of water in toluene is 0.006 mole percent at 10°C. Toluene is miscible with alcohol, ether, benzene, and acetone (4). Other physical properties of toluene may be found in Table I (1, 2, 3, 4, 5, 6).

The stability of toluene is a contributing factor to its widespread use as a solvent. In this function, it is employed in both the chemical and pharmaceutical industries, either as a starting material or as an intermediate in chemical synthesis. Uses as an intermediate include the manufacturing processes for trinitrotoluene (TNT), benzaldehyde, and benzoic acid. Toluene is also used as a thinner for paints, varnishes, enamels, and lacquers, and as a constituent in motor and aviation fuel. Toluene is added to motor

TABLE I

PHYSICAL PROPERTIES OF TOLUENE

Molecular formula	$C_6H_5CH_3$
Physical state	liquid
Molecular weight	92.13
Boiling point	110.623°C
Freezing point	-94.991°C
Vapor pressure	30 mm at 26.04°C 28 mm at 25°C
Specific gravity	0.86220 (25°/4°C)
Vapor density (air = 1)	3.14
Percent in saturated air 760 mm	3.94 (26°C)
Density of saturated vapor-air mixture at 760 mm (air = 1)	1.09 (26°C)
Specific dispersion	184.4
Solubility in water	0.047 g/100 ml (16°C)
Solubility of water in toluene	0.006 mole percent (10°C)
Flammable limits (percent by volume in air)	1.17 - 7.10
Flash point (closed cup)	40°F
Autoignition temperature	552°C
Odor	200 ppm ≈ intensity of 3
Conversions:	1 mg/l ≎ 266 ppm 1 ppm ≎ 3.76 mg/m^3 at 25°C 760 mmHg
Refractive index	1.497 (20°C)

TABLE I (CONCLUDED)

Partition Coefficient (octanol/water)	2.525 average
Odor Threshold in air	4.68 ppm (coke derived) 2.14 ppm (petroleum derived)
Dipole moment	0.35 ($x10^{18}$) e.s.u.
Specific heat	0.4041 at 20°C
Surface tension	28.53 dynes/cm at 20°C
Heat of vaporization	9.08 kcal/mole at 25°C
Liquid Viscosity	0.6 cp at 20°C
Heat of fusion	1.582 kcal/mole
Heat of formation	11.950 kcal/mole (gas) 2.867 kcal/mole (liquid)
Cricital temperature	320.8°C
Critical pressure	40 atm
Critical density	0.29 g/ml

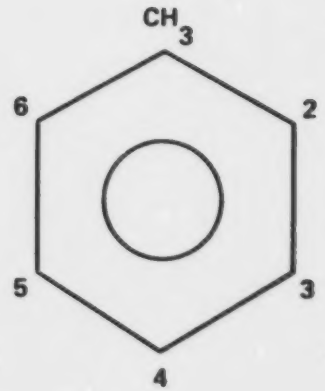
fuels as an anti-knock agent which enables the fuel to be used for high performance engines (3, 7).

The nucleus of toluene, like that of benzene, undergoes substitution of hydrogen, either on the aliphatic side-group ($-CH_3$) or on the aromatic ring ($-C_6H_5$). This substitution occurs almost exclusively at the ortho (2) and para (4) positions (see Figure 1). As with benzene, toluene is capable of giving either monosubstituted or multi-substituted products under contrived conditions. The hydrogen atoms of the $-CH_3$ group may be replaced by halogen at high temperatures in the presence of ultra-violet light. As noted previously, toluene is quite stable and these chemical reactions normally require the presence of an unusual force, e.g., temperature or pressure extremes (3, 4).

Toluene is relatively unreactive toward RO_2 and O_3 ($t_{1/2}$ = 10^5 - 10^6 days) but is reactive toward HO. The relative rate of oxidation by HO is .05, by RO_2 is 5.90, and by O_3 is 4.60. The products of this reactivity are normally benzaldehyde and cresols (6). Exposure to toluene can be either to the relatively pure substance or as a component of solvent mixtures. Industrial and 90/120 grades of toluene can contain up to 25 percent benzene, which may possibly result in a benzene concentration of 50 percent in the vapor (1).

Azeotropes, which limit toluene purification, are also pertinent to solvent technology and to the recovery of toluene from reaction mixtures. The most important toluene azeotropes are listed, with

FIGURE 1
THE STRUCTURAL FORMULA FOR TOLUENE



boiling points, in Table II (8). All of those listed are minimum boiling; that is, the boiling point of the azeotrope is lower than that for either of the constituents.

The similarities existing between benzene and toluene are such that relative reactivity in substitution reactions has been determined. Table III contains a compilation of various substitution reactions with reactivity ratios which have been determined for toluene/benzene (9). As is evidenced by the table, toluene adapts more readily to substitution reactions than does benzene. This is due to the presence of the methyl group which offers an additional reaction possibility. At one time, the most significant use of toluene was hydrodealkyation to produce benzene (9).

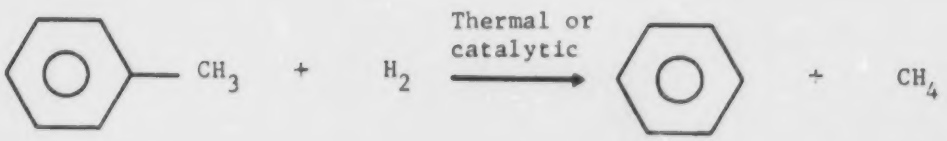


TABLE II

AZEOTROPES OF TOLUENE

Component	bp, °C	Azeotrope		
		bp, °C	Component, wt %	Toluene, wt %
paraffins				
n-heptane	98.4		nonazeotrope	
2,5-dimethylhexane	109.4	107.0	65	35
2,3,4-trimethylpentane	113.5	109.5	40	60
2-methylheptane	117.6	110.3	18	82
n-octane	125.4		nonazeotrope	
naphthenes				
methylcyclohexane	100.85		nonazeotrope	
ethylcyclopentane	103.5	103.0	93	7
1,1,3-trimethylcyclopentane	104.9	103.8	84	16
cis,trans,cis-1,2,4-trimethylcyclopentane	109.3	107.0	61	39
cis,trans,cis-1,2,3-trimethylcyclopentane	110.4	108.0	61	39
cis-1,3-dimethylcyclohexane	120.1	110.6	4	96
1.3-dimethylcyclohexane	120.7		nonazeotrope	
hydroxyl compounds				
methyl alcohol	64.7	63.8	69	31
ethyl alcohol	78.3	76.7	68	32
isopropyl alcohol	82.4	80.6	58	42
n-propyl alcohol	97.2	92.6	43	57
water	100.0	84.1	13.5	86.5
sec-butyl alcohol	99.5	95.3	55	45
n-butyl alcohol	117.8	105.5	32	68
2-pentanol	119.8	107	28	72
3-pentanol	116.0	106	35	65

Adapted from "Azeotropic Data," Advances in Chemistry, Series 6, 1952.

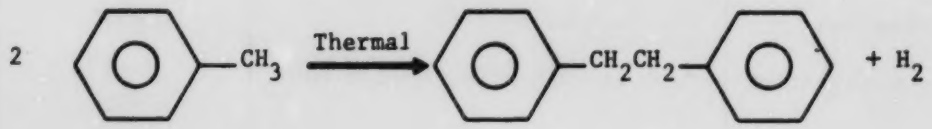
TABLE III

RELATIVE RATES OF SUBSTITUTION IN BENZENE AND TOLUENE

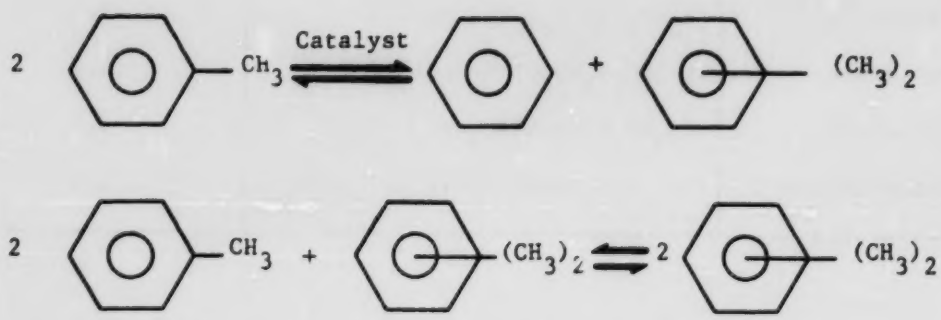
Reaction	Conditions	$k_{toluene}/k_{benzene}$ Reactivity ratio
Bromination	Br_2 in HOAc with I_2 at 25°C	467
	Br_2 in HOAc with I_2 at 45°C	272
Chlorination	Cl_2 in HOAc at 24°C	353
Chloromethylation	CH_2O in HOAc at 60°C with $ZnCl_2$ and HCl	112
Nitration	$AcONO_2$ in Ac_2O at 0°C	27
	$AcONO_2$ in Ac_2O at 30°C	23
	HNO_3 in CH_3NO_2 at 30°C	21
Acetylation	AcCl with $AlCl_3$ at 0°C	13.3
	AcCl with $AlCl_3$ at 50°C	8.4
Benzylation	BzCl with $AlCl_3$ at 25°C	120-200
Mercuration	$Hg(OAc)_2$ in HOAc with $HClO_4$ at 25°C	7.9
	at 50°C	7.0
	at 75°C	5.9
Sulfonation	H_2SO_4 in $C_6H_5NO_2$ at 40°C	5.1
Bromylation	$p\text{-}BrC_6H_4SO_2Cl + AlCl_3$	3.7
Methylation	CH_3Br with $AlBr_3$ at 0°C	3.5
Isopropylation	CH_3CHCH_2 with $AlCl_3$ in CH_3NO_2 at 40°C	2.1

Adapted from: Kirk, Othmer, eds., The Encyclopedia of Chemical Technology, Vol. 20, 1964.

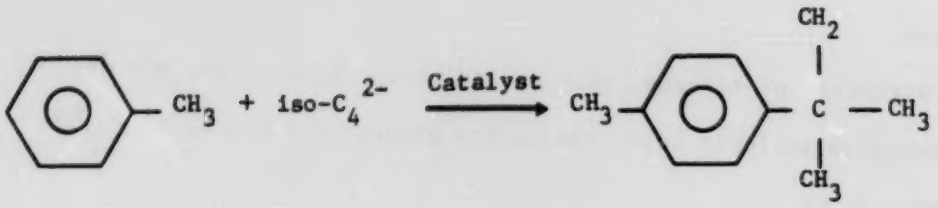
Many other synthetic commercial processes have been devised and utilized for toluene. They are all conducted in the vapor-phase at high temperatures under greater than 20 atm pressure. The formation of dibenzyl occurs under appropriate thermal conditions (9).



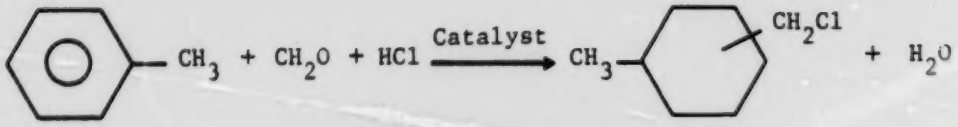
Disproportionation and transalkylation in the presence of a catalyst are also economically significant reactions that are reversible and can be executed in either the liquid or vapor phase (9).



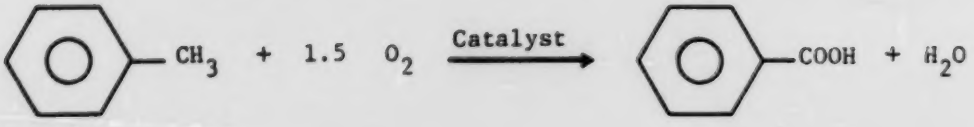
Alkylation in the presence of an acidic catalyst,



as well as chloromethylation occurs readily (9).

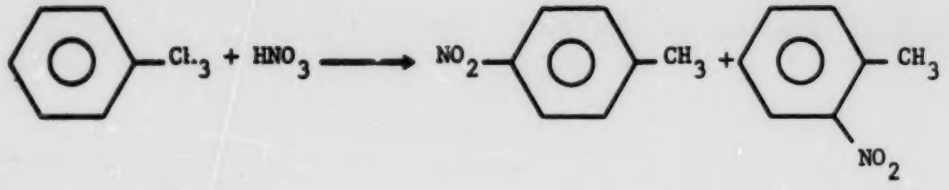


Oxidation of liquid phase toluene, using a catalyst, yields benzoic acid as a principal product (9).

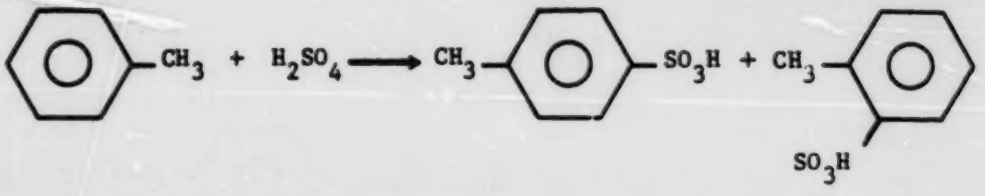


Oxidation of the methyl group can also be accomplished with various oxidizing agents; however, these are not utilized in commercial applications.

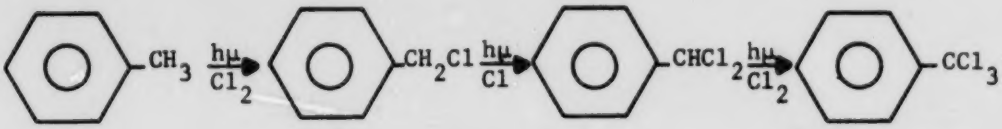
Nitration of toluene, with strong nitric acid in the presence of concentrated sulfuric acid, has as its product a mixture of o- and p-nitrotoluene (9).



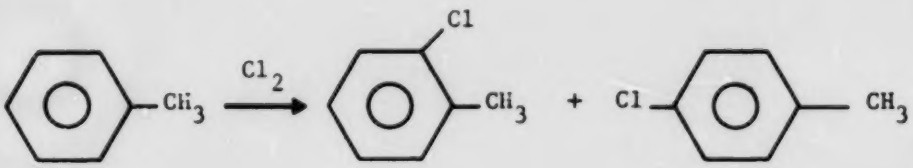
Sulfonation of toluene also produces the o- and p-toluenesulfonic acids in a mixture (9).



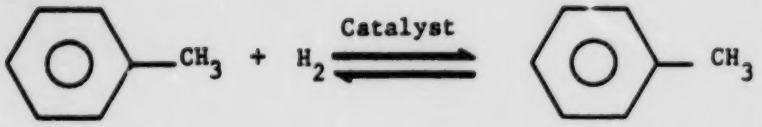
Halogenation of toluene occurs by substitution. As an example, chlorine and toluene react to yield methyl substitution products upon exposure to actinic light (9).



The presence of a catalyst and the absence of light in this same reaction produce o- and p-chlorotoluenes (9).



Hydrogenation to form methylcyclohexane, a naphthene, occurs readily and is reversible. The dehydrogenation of methylcyclohexane is the principal mode of toluene manufacture, as the naphthene is found in petroleum fractions along with other naphthenes and is concentrated by distillation and then dehydrogenated to toluene (9).



B. EFFECTS

1. Humans

Many reports of toluene toxicity compare the symptoms and effects to benzene toxicity (10, 11, 12, 13, 14). Because of the probable contamination of toluene with benzene in many industrial situations, purity must be carefully considered before attributing adverse reactions to toluene alone (15, 16, 17). Much of the experimental data prior to the 1940's in the United States and up to the mid 1950's in other parts of the world are doubtful in regard to validity due to lack of availability of pure toluene. Although toluene had been reportedly toxic in 1903, the possibility of benzene causing the attributed effects was not recognized until much later (5, 18).

The primary mode of exposure to toluene is vapor inhalation, with oral and dermal exposure generally only accidental. Daily oral doses of 10 grams in olive oil have been administered to humans for 3 weeks without adverse symptoms reported or clinically diagnosed, thereby indicating the innocuous nature of toluene (19). Toluene readily dissolves fat; therefore, dermal contact will remove natural lipids, causing dryness, fissures and dermatitis* (20). However, liquid toluene absorption through the skin occurs slowly, 14 to 13

*Inflammation of the skin evidenced by itching, redness and various skin lesions.

mg/cm^2/hour (21). Gerarde (20) found this liquid absorption through the skin so slow that systemic intoxication would be improbable. Piotrowski (22) found the dermal absorption of toluene vapor to be 5 percent or less of the amount absorbed through the respiratory tract. Eye irritations have been reported due to vapor and liquid exposure. Minor corneal damage and conjunctival irritation,* transient epithelial injury and a burning sensation were noted, with abatement occurring within 48 hours (23, 24, 25, 26).

One of the most common effects of acute toluene inhalation is anesthesia due to its affinity for the brain lipids. Other effects on the central nervous system were reported in a study using pure toluene, with exposures of eight hours, twice weekly, for three months. The symptoms noted were as follows (27, 28):

0 ppm--occasional slight fatigue probably due to lack of exercise, monotonous noise, and poor illumination.

50 ppm--drowsiness with very mild headache. No aftereffects.

100 ppm--essentially the same as 50 ppm.

200 ppm--muscular weakness, confusion, impaired coordination, pupil dilation, impaired light accommodation, prickling and burning sensation of the skin, repeated headache, and nausea. Fatigue, moderate insomnia, restless sleep, and general confusion were reported as aftereffects.

300 ppm--severe fatigue, headache, incoordination, muscular weakness, and slight pallor. Aftereffects included fatigue, insomnia, headache, and paresthesias of the skin.

*Inflammation of the mucous membranes lining the eye.

400 ppm-- fatigue, mental confusion, dilated pupils, headache, muscular weakness, skin paresthesias*. After effects were fatigue, insomnia, headache, skin paresthesias.

600 ppm--extreme fatigue, exhiliration, nausea, mental confusion, severe headache, and dizziness after three hours. After eight hours staggering gait and incoordination. Nervousness and some confusion were after effects.

800 ppm--extreme nausea, confusion, severe fatigue, lack of self-control, staggering gait and considerable incoordination after three hours. Moderate to severe insomnia lasting several days was noted as an after effect.

There were no changes observed in white cell blood count at any concentration. The lack of effects under 200 ppm was supported by another researcher (29).

In another study, two males were exposed to known toluene concentrations for 7 to 8 hours. Symptoms reported were (24):

200 ppm--mild eye and throat irritation and slight exhiliration

400 ppm--nausea, hilarity, lassitude**, mild eye irritation. lacrimation***

600 ppm--verbosity, boisterousness, hilarity, lassitude. Anorexia****, and listlessness reported as after effects.

800 ppm--headache, extreme lassitude, metallic taste, scotomata*****, verbosity, nausea, and "inebriation"

In a case of toluene habituation, acute intoxication was characterized by "inappropriate" speech, headache and brief losses of memory.

---

*Abnormal sensations without objective causes such as numbness, tingling, prickling.

**Exhaustion.

***Secretion and discharge of tears.

****Loss of appetite.

*****Areas of dimmed vision.

Clinical and laboratory studies indicated no pathological abnormalities (30). A report of permanent encephalopathy* due to repeated exposure to toluene vapor for 14 years appeared in 1966. A 33-year old man had purchased pure toluene for 14 years in order to indulge his addiction to the vapor. He typically began each day with inhalation of several breaths taken from a toluene-soaked cloth until reddening of vision and light-headedness occurred. This procedure was frequently repeated during each day. Permanent cerebral atrophy appeared, evidenced by ataxia**, emotional lability, tremulousness, distorted nostrils on subjection to sniff test, and positive Babinski toe reflex on the right side. Electroencephalography and pneumoencephalography confirmed the damage (31).

Cerebral electric potential has been reported to increase upon brief exposure to toluene vapor. Exposure to 1.5 mg/m^3 (0.399 ppm) enhances brain electrical potential (32), while a concentration of 0.6 mg/m^3 (0.159 ppm) is subliminal (33). The significance of the enhancement of brain electropotential is uncertain. It is only clear that it is a measurable effect produced by toluene at this concentration. This subliminal level is suggested by the investigator as the maximum one-time concentration permissible.

Changes in production of total serum glycoproteins, serumucoid, or haptoglobulins in 53 women exposed during working hours to an

---

*Brain dysfunction.
**Muscular incoordination.

average concentration of 0.25 mg/l (67 ppm) industrial toluene were reported. All women showed abnormal production of at least one of the three substances, accompanied by no clinical or laboratory evidence of liver changes or altered liver function (13). Cases of hepatorenal* damage due to toluene vapor exposure have been reported. Serious, but reversible, injury to the kidneys and liver was noted in a 19-year old male "glue sniffer" (34). Twenty-one percent of the painters examined in an earlier study exhibited hepatomegaly** while only seven percent of the control group (unexposed fur workers) had enlarged livers (35). All of these three studies pertained to toluene exposure of questionable purity. A study of workers exposed to toluene of undetermined purity reported mild intoxication, macrocytosis***, slightly reduced erythrocyte level, elevation of hemoglobin, enlarged livers, and absolute lymphocytosis**** (35). An increase in prothrombin content of the blood and a decrease in phagocytic activity***** of the polymorphonuclear leukocytes have been related to industrial toluene exposure (36, 37).

Changes in peripheral blood chromosomes due to toluene exposure have been investigated. Workers in a rotogravure plant, exposed to concentrations of 200 ppm with occasional concentrations much higher,

---

*Liver and kidney.
**Liver enlargement.
***Production of larger than normal erythrocytes.
****Excess lymph cells.
*****Ingestion and destruction of foreign particulate matter.

showed an elevated rate (0.8%) of unstable chromosome aberrations and of calculated breaks (0.83%). However, the effect is not statistically significant when compared with the controls who exhibited an elevated rate of 0.61% and a rate of 0.67% for calculated breaks (38).

The myelotixic effect of toluene has been the subject of persistent controversy. The majority of this opinion difference is most likely due to investigations of exposure to benzene-contaminated toluene, with the current evidence indicating that toluene alone is not myelotoxic (16, 17). A study reported in 1954 found that no particular bone marrow toxicity or adverse effect on other organs in workers exposed to ambient toluene concentrations of 200-800 ppm (39). Particularly convincing evidence of the lack of myelotoxicity is presented by Francone and Braier (19). Toluene, because of its supposed myelotoxic action, was administered orally as a treatment for leukemia. The patients tolerated the toluene with no adverse side effects, but also, unfortunately, with no remission or reduction in the progress of the disease in their bone marrow.

The effect of toluene vapor on the peripheral blood emerged in 1969. Printers and helpers from a rotogravure plant, who had been exposed for over 3 years to vapors from printing inks containing toluene but no chemically detectable benzene, were subjected to extensive blood studies with a few accompanying bone marrow evaluations. Hemoglobin, leukocyte, erythrocyte and granulocyte determinations revealed no effects on the formed elements of the blood. Only

3 of the 889 blood tests had white cell counts less than 4000/cu mm (0.33%) as compared with 1 of the 155 control tests from other departments in the plant (0.64%). Absolute lymphocyte counts never exceeded 5,000, while absolute granulocyte counts were never below 2,000 in either the printers or in the controls. Five sternal biopsies also disclosed no pathological alterations of the bone marrow (16). Another evaluation reported no blood picture or liver function changes after performing hemoglobin, erythrocyte, leukocyte and platelet evaluations on laborers chronically exposed to toluene vapor ranging in concentration from 80-300 ppm (23). This report is supported by current evidence from studies using purified toluene which have found no toxic action on the blood or blood-forming organs (17, 23, 38, 39, 40, 41, 42).

No evidence for positive carcinogenic action of toluene in humans was found in the literature. Table IV contains a summation of the relevant effects of toluene on humans.

Toluene is much more soluble in fat than in blood, having tissue-blood partition coefficients of 1-3 (43). Due to its liposolubility, toluene is accumulated mainly in lipoid-containing organs, such as adrenal gland, bone marrow and brain. The circulating blood rapidly equilibriates with the toluene vapor in the air, due to the low solubility of toluene in blood (44).

Toluene is metabolized mainly by oxidation of its methyl group to benzoic acid which later becomes water soluble by conjugation with

TABLE IV

EFFECTS OF TOLUENE EXPOSURE ON HUMANS AND ANIMALS

Organism	Mode of exposure	Concentration of exposure	Duration of exposure	Effects	Reference
Human	Oral	10 g/day	3 weeks	None reported; no bone marrow toxicity	17
Human	Inhalation	50 ppm	8 hours/day 2 days/week 3 months	Drowsiness with mild headache, no after effects	28
		100 ppm	"	Drowsiness with mild headache, no after effects	28
		200 ppm	"	Muscular weakness, confusion, impaired coordination, pupil dilation, impaired light accommodation, prickling and burning sensation of the skin, repeated headache and nausea. Fatigue, moderate insomnia, restless sleep and general confusion were reported as after effects.	28
		300 ppm	"	Severe fatigue, headache, incoordination, muscular weakness and slight pallor. After effects included fatigue, insomnia, headache and paresthesias of the skin.	28
		400 ppm	"	Fatigue, mental confusion, dilated pupils, headache, muscular weakness, skin paresthesias. After effects were fatigue, insomnia, headache, skin paresthesias.	28
		600 ppm	"	Extreme fatigue, exhiliration, nausea, mental confusion, severe headache, and dizziness after three hours. After eight hours, staggering gait and incoordination. Nervousness and some confusion were after effects.	28
		800 ppm	"	Extreme nausea, confusion, severe fatigue, lack of self-control, staggering gait and considerable incoordination after three hours. Moderate to severe insomnia lasting several days was noted as an after effect.	28
Human	Inhalation	200 ppm	7-8 hours	Mild eye and throat irritation and slight exhiliration.	24
		400 ppm	"	Nausea, hilarity, lassitude, mild eye irritation, lacrimation	24

TABLE IV (Cont'd)

Organism	Mode of exposure	Concentration of exposure	Duration of exposure	Effects	Reference
Human	Inhalation	600 ppm	7-8 hours	Verbosity, boisterousness, hilarity, lassitude; anorexia and listlessness as after effects.	24
		800 ppm	"	Headache, extreme lassitude, metallic taste, scotomata, verbosity, nausea and inebriation.	24
Human	Inhalation	Very high, but incalculable	Daily for 14 years	Reddening of vision and lightheadedness upon exposure; permanent cerebral atrophy confirmed by ataxia, emotional lability, tremulousness, distorted nostrils during sniff test, and positive Babinski toe reflex on the right side.	31
Human	Inhalation	1.5 mg/m^3 (0.398 ppm)	Acute	Enhances brain electropotential.	32
Human	Inhalation	0.6 mg/m^3 (0.159 ppm)	Acute	No brain electropotential enhancement.	33
Human	Inhalation	Normally 200 ppm	During working hours	An elevated rate of unstable chromosome aberrations, not statistically significant.	38
Human	Inhalation	200-800 ppm	During working hours	No bone marrow toxicity.	39
Human	Inhalation	80-300 ppm	During working hours	No blood or liver function alterations.	23
Human	Inhalation	Vapors from printing inks	3 or more years	No hematopoietic system damage or myelotoxic effects.	16
Human	Inhalation	100-200 ppm	18 hours	68% of the absorbed toluene excreted as hippuric acid.	46
Rats	Inhalation	30-1000 mg/m^3 (7.97-265.95 ppm)	Chronic	Latency period before manifestation of toxic effects, increasing as toluene concentration decreases.	52
Rats	Inhalation	50 mg/l (13,300 ppm)	2 hours	Absolute lethal dose.	50
Rats	Subcutaneous injection	7 g/kg	Acute	Absolute lethal dose.	50

TABLE IV (Cont'd)

Organism	Mode of exposure	Concentration of exposure	Duration of exposure	Effects	Reference
Rats	Oral	8 g/kg	Acute	Absolute lethal dose.	50
Rats	Inhalation	50 mg/l (13,300 ppm)	Acute	Lethal dose.	51
Rats	Inhalation	49.6 mg/m^3 (13.19 ppm)	5 hours/day 6 days/week 6 months	Increase in protein synthesis.	63
Rats	Inhalation	153 mg/m^3 (40.69 ppm)	5 hours/day 2 days/week 6 months	Diminished protein synthesis.	63
Rats	Inhalation	200 ppm 1000 ppm 2000 ppm	3 hours/day 32 weeks	No significant change in body weight or hematological determinations.	40
Rats	Injection	1 mg/kg	Repeated	No abnormalities in weight of the thymus or spleen, in total number of nucleated bone marrow cells, or in peripheral blood leukocytes.	57
Rats	Injection	1 mg/kg/day	12 weeks	Bone marrow, chromosome damage.	59
Rats	Injection	0.8 g/kg/day	12 days	Stimulation of neutropoiesis, chromosome breaks, metaphase aberrations.	60
Rats	Inhalation	0.5 mg/l (133 ppm) 0.05 mg/l (13.3 ppm)	Chronic	Change in chronaxial relationship between antagonistic muscles, decrease in cholinesterase, leukocytosis and reticulocytosis at the higher concentration, immunological inhibition at both levels.	61
Rats	Inhalation	50 mg/m^3 (13.29 ppm)	5 hours/day 1-6 months	Initial increases in serum protein with a decrease in serum ascorbin acid and liver riboflavin.	62,64
Mice	Inhalation	35 mg/l (9310 ppm)	Acute	Lethal dose.	51
Mice, rats	Inhalation	1 mg/l (266 ppm)	Acute	Threshold dose affecting the nervous system.	51

TABLE IV (Concluded)

Organism	Mode of exposure	Concentration of exposure	Duration of exposure	Effects	Reference
Mice	Inhalation	10 mg/l (2660 ppm)	Acute	Animals fell on their sides.	51
Mice	Inhalation	25 mg/l (6650 ppm)	Acute	LD-50	51
Mice	Inhalation	5300 ppm	8 hours	Minimum lethal concentration.	54
Mice	Inhalation	800 ppm	30 minutes	No abnormal resistance to hemolysis.	54
Guinea pigs	Inhalation	1250 ppm	4 hours/day 18 days	Severe prostration.	53
Guinea pigs	Inhalation	4000 ppm	---	Death.	53
Guinea pigs	Inhalation	1000 ppm	35 days	No reported effects.	53
Dogs	Inhalation	2000 ppm	8 hours/day 6 days/week 4 months for	No hematological malfunctions.	39
		and 2600 ppm	2 more months	Central nervous system intoxication, incoordination and hind leg paralysis.	
Rabbits	Dermal	Undilute	Acute	Slight conjunctival membrane irritation.	65
Rabbits	Injection	300 mg/kg/day	6 weeks	No depression in bone marrow function or changes in peripheral blood.	58
Rabbits	Injection	700 mg/kg/day	9 weeks	No depression in bone marrow function or changes in peripheral blood.	58
Rabbits	Inhalation	0.5 mg/l (133 ppm) 0.05 mg/l (13.3 ppm)	Chronic	Change in chronaxial relationship between antagonistic muscles; decrease in cholinesterase, leukocytosis and reticulocytosis at the higher concentration; immunological inhibition at both levels.	61

glycine and is finally eliminated in the urine in the form of hippuric acid. This is the fate of approximately 80 percent of the absorbed

$$C_6H_5COOH + NH_2CH_2COOH \quad C_6H_5CONHCH_2COOH + H_2O$$

(benzoic acid and glycine hippuric acid and water)

toluene, with the remaining absorbed toluene eliminated unaltered via exhalation. Oxidation of the aromatic ring to phenol compounds is also possible, but has not been reported (44, 45). Excretion of hippuric acid, as a metabolity of toluene, occurs rapidly, In an eighteen-hour experiment of controlled exposure to 100 and 200 ppm, the amount of excreted hippuric acid was equivalent to 68 percent of the absorbed toluene (46).

Urinary hippuric acid excretion has been purported to be proportional to the toluene concentration in the inhaled air. Exposure to 50 ppm led to an excretion level 3.4 times the pre-exposure level, while 20 ppm led to a level 1.9 times the pre-exposure level (47). However, there have been a relatively wide range of hippuric acid excretion levels reported after exposure. Pagnotto and Lieberman (48) found a mean value of 3.66 grams hippuric acid/liter urine in workers exposed to an average of 73 ppm toluene. An average of 2.84 grams/liter was reported after exposure to 125 ppm (49) while exposure to 200 ppm toluene produced 7 grams/liter (48). Dietary habits can provide a reason for the variabilities observed. Gerarde emphasized the detection of hippuric acid as a normal metabolite of foods containing benzoates or benzoic acid (20). Therefore, hippuric

acid measurement would not be a sufficient method for determination of exposure.

2. Animals

The primary effect of toluene on laboratory animals closely parallels the major effect observed in humans, disturbance of the central nervous system, with a primary mode of exposure being inhalation. A latency period, before the manifestation of toxic effects, has been demonstrated to increase in rats with a graded reduction of toluene concentration (from 100-30 mg/m^3 or 265.95-7.97 ppm). This latency period lengthens further with increased time intervals between exposures (52).

A variation in absolute lethal dosage of toluene in rats was noted, dependent upon method of exposure. In inhalation experiments, 50 mg/l (13,300 ppm) for 2 hours proved sufficient. Seven g/kg was required to induce lethality subcutaneously, while an absolute lethal dose of 8 g/kg was established for oral administration (50). Acute experimental intoxication indicated a lethal inhalation dose of 35 mg/l (9310 ppm) for mice and 50 mg/l (13,300 ppm) for rats. A threshold dose affecting the central nervous system was 1 mg/l (266 ppm). A concentration of 10 mg/l (2660 ppm) caused mice to fall on their side, while an LD_{50} of 25 mg/l (6650 ppm) was established (51).

Demonstration of the hematopoietic* toxicity of toluene has been attempted. Distillation-purified toluene caused severe prostration,

* Related to the tissues responsible for formation of constituents of blood.

but no fatalities, in guinea pigs after 18 four-hour daily exposures to 1250 ppm. Exposures to 4000 ppm did cause mortality, but exposure to 1000 ppm for 35 days resulted in no reported effects (53). Dogs exposed 8 hours/day, 6 days/week, for four months to 2000 ppm of 99.9 percent pure toluene vapor and then to 2660 ppm for two additional months, showed no hematological manfunctions. Central nervous system intoxication, incoordination and hind leg paralysis were observed during the two final months (39). Rats exposed to 200, 1000, and 2000 ppm of 99.9 percent pure toluene vapor 8 hours/day for 32 weeks exhibited no significant changes in body weight or hematological determination (leukocyte, eosinophil and erythrocyte counts and hemoglobin levels) (38). A minimum lethal concentration in mice of 20 mg/liter (5300 ppm) for an 8-hour exposure was established by Svirbely et al. (53). They concluded that the narcotic action and toxicity of toluene was greater than benzene; however, no evidence of hematological damage was found. The erythrocytes of mice exposed to 800 ppm toluene for 30 minutes exhibited no abnormal resistance to hemolysis* although this concentration is four times the maximum allowable limit recommended by the National Institute for Occupational Safety and Health (54). This recommendation states that occupational exposure of workers to toluene shall not exceed

*A destruction of red blood cells accompanied by the release of hemoglobin into the surrounding fluid.

100 ppm (375 mg/m^3) determined as a time-weighted average exposure during an 8-hour day with a ceiling of 200 ppm (750 mg/m^3) as determined by a 10-minute sampling time (55). All of the above animal studies indicate the absence of toluene toxicity on the hematopoietic system. However, a 40 mg/l (10,640 ppm) concentration of toluene, purity undetermined, inhaled for 2 hours each day for 30 days induced a leukocytic reaction accompanied by neutrophilia* and lymphopenia** in rabbits. The same symptoms with the addition of absolute eosinophilia*** were evidenced in rats (56).

Possible myelotoxic effects of toluene have been investigated. After repeated subcutaneous injections into rats of 1 mg/kg pure toluene, the effects on blood, thymus, bone marrow and spleen were noted. No abnormalities were reported in the weight of the thymus glands or spleen, in the total number of nucleated bone marrow cells, or in the peripheral blood leukocyte count (57). In rabbits, subcutaneously injected pure toluene resulted in no depression of bone marrow function or changes in peripheral blood at doses of 300 mg/kg/day for six weeks or 700 mg/kg/day for nine weeks. It was felt that this evidence substantiated the lack of toluene myelotoxicity (58). However, in a test for the mutagenicity of toluene, positive evidence of bone marrow chromosome damage was found. Aberrations were induced in rats dosed with toluene at a level of

*Increase in the number of neutrophil leukocytes.
**Deficiency of lymphocytes in the blood.
***Accumulation of cells that readily stain with an acid stain (eosin).

1 mg/kg body weight injected subcutaneously, daily for twelve days (59). A similar subcutaneous administration of 0.8 g/kg for 12 days stimulated neutropoeisis* and induced metaphase aberrations and chromosomal breaks in the lamina cells of bone marros(60).

In a study of prolonged chronic exposure to low toluene concentrations. rats and rabbits were dosed with both 0.5 (133 ppm) and 0.05 (13.3 ppm) mg of toluene per liter of air. Alterations in central nervous system function were exemplified by changes in the chronaxial** relationship between antagonistic muscles and a decrease in cholinesterase activity. Hematological tests did suggest leukocytosis*** and reticulocytosis**** at the higher concentration while no morphological changes occurred in the animals receiving 0.05 mg/l (13.3 ppm). A decrease in the phagocytic activity of leukocytes and in the agglutination titer of the blood serum indicated inhibition of immunological reactivity at both levels (61). Rats exposed to 50 mg/m^3 (13.29 ppm), 5 hours/day, for one-to-six months experienced initial increases in serum protein levels and decreases in serum ascorbic acid and liver riboflavin concentrations. After four months, these levels returned to normal; however, elevated immunobiological activity and oxygen uptake remained (62).

---

*Formation and development of neutrophils.
**Nerve sensitivity to electrical stimulation.
***Increase in the number of white blood cells.
****Increase in the number of immature red blood cells.

Adaptation to the metabolic effects of toluene poisoning was observed in rats chronically exposed by inhalation to 49.6 mg/m^3 (13.19 ppm), 5 hours/day, 6 days/week for 6 months. This adaptation involved an increase in protein synthesis, due primarily to an increase in serum globulins, and intensified toluene detoxification in the liver. Exposure to 153 mg/m^3 (40.69 ppm), 5 hours/day, 2 days/week, for 6 months revealed a markedly diminished rate of protein synthesis and a deficiency of available amino acids which led to impaired toluene detoxification (63). Monitoring of serum protein levels in rats during inhalation of 50 mg/m^3 (13.29 ppm), 5 hours/day, for 6 months, revealed an increase during the first four months. Serum ascorbic acid and liver riboflavin initially decreased but returned to normal after 4 months as did the serum protein levels (64).

Limited studies of the dermal effects of toluene in animals were found. In a case of direct application to the eye in rabbits, undiluted pure toluene induced a barely perceptible conjunctival membrane irritation with no evidence of even superficial necrosis* in three of the six animals tested (65).

No positive evidence for the carcinogenicity of toluene in animal species was found in the literature. It is possible, however, that administration of the hydrocarbon has not been of a sufficient duration or dosage to induce tumors.

---

*A gradual degeneration or death of an area of tissue.

An investigation of the effects of toluene in rats was published in 1956. A total of 138 daily feedings at levels of 118, 354 and 590 mg/kg body weight were administered by gastric intubation. Observation of the test animals for 193 days revealed no tumors or tissue histopathology (66).

Dermal exposure has similarly produced no observable tumors. In three strains of mice, painted with 7.5 µl of toluene, 3 times per week for life, no evidence for the carcinogenicity of the compound was revealed (67). One investigation did produce a report of one permanent and one regressing (of three weeks' duration) tumor in 14 animals. Unfortunately, toluene was utilized as a solvent control in this study and, as a result, there was no completely untreated control group. A group of 23 mice in this study treated once with DMBA* developed no tumors. However, it was felt that the experimental duration was too short and that the numbers of animals involved were not statistically significant (68). See Table IV for a compilation of the reported toxicity of toluene in animals.

The affinity of toluene for lipoid containing organs is due to the enhanced solubility of toluene in fat. As in man, toluene has been found accumulated primarily in lipoid-containing organs in animals. Transmission of toluene into the brain and placenta has been shown to follow intramuscular injection and subsequent distribution in mice (69).

*dimethoxybenzaldehyde.

In animals, as in humans, approximately 80 percent of the absorbed toluene is converted to benzoic acid, conjugated with glycine and excreted in the urine as hippuric acid while approximately 20 percent is excreted, unaltered, by the lungs. Ortho- and paracresol, hydroxylated from toluene, were found accountable for 0.4 to 1.1 percent of the absorbed toluene that is eliminated through the urine. Benzyl alcohol, which may be an intermediate during benzoic acid production, was also detected (70). An increase in the excretion of organic sulfate, after large subcutaneous doses, was reported, indicating that an additional metabolic pathway could be used to detoxify toluene in rats (71). The need for this alternative metabolic method in rats may be explained by the poor excretion of toluene metabolites in the bile (72). Enhanced hepatic metabolism induced by phenobarbital, has been found to increase the rate of toluene elimination from the blood and to reduce the sensitivity of the central nervous system to toluene's deleterious effects (73).

3. Other Effects

Examination of the effect of a 10 ppm concentration of toluene on the giant kelp, Macrocystis phrifera, revealed a greatly reduced photosynthetic rate (74). Currier reported that the toxicity of toluene exceeded that of benzene with respect to herbicidal properties. Working with water to paraffin oil partition coefficients, an inverse relationship between toxicity and compound solubility was reported. Cellular pentration, and, therefore, toxicity was concluded

to be directly related to the number of methyl groups on the benzene ring (75).

Toluene toxicity and its effects have been established for some microorganisms. Threshold toxicities of 60 ppm, 120 ppm and 200 ppm were established for Daphnia, Scenedesmus and Escherichia coli, respectively (76). E. coli, after treatment with 0.25% toluene, exhibited partial plasma membrane dissolution and displacement of nuclear material toward the cellular periphery (77). Lysis, as determined by electron microscopy, did not occur, although the cytoplasm was observed to collapse into the cell. The material lost, due to this collapse, contained 85% of the total cellular RNA, the majority of which was Ribosomal (78). Toluene disrupted the internal cellular morphology of Chlamydomas reinhardtii while the outer membrane remained intact (79). However, the cytoplasmic membranes of Saccharomyces cerevisiae were attacked by toluene (80). A final concentration of 0.4% toluene completely sterilized a urine sample containing E. coli and Pseudomonas fluorescens within 24 hours of the addition of the toluene (81).

The ability of microorganisms to utilize and degrade toluene has been reported. Toluene, at low concentrations, decreases the light emissions from Vibrio luminosus, indicating a reduced metabolic rate of the bacteria due to toxicity (64). Evidence for biodegradation of toluene in activated sludge treatment systems was reported by Buzzell et al. It was found that 10 mg/l (2660 ppm) concentrations

of toluene in aquatic systems were reduced by 32% within 20 days of inoculation with sewage sludge microorganisms (BOD_{20} = 32% of the theoretical) (82). A pseudomonas-type bacteria was isolated from the soil of a petroleum deposit which utilized toluene as a source of carbon (83). Pseudomonas and Achromobacter from soil can use toluene as the sole carbon source for growth (84,85).

Metabolic pathways for bacterial oxidation of toluene were elucidated by Gibson (1972). The hydrocarbon is either enzymatically converted to benzoic acid by oxidation of its methyl group or ring hydroxylated directly to form 3-methylcatechol as the end product. At times, orthocresol has been detected as a nonenzymatically formed metabolite (86).

Radioactive carbon-labelled toluene was not metabolized by the mussel Mytilus edulis and was released from its tissues upon transfer to fresh seawater. Concentrations up to 1 ppm did not have a lethal effect on the invertebrate; however, filtration ability may have been inhibited due to a chemoreceptor detection of the hydrocarbon and subsequent filtration rate modification (87).

The acute toxicity of toluene to aquatic vertebrates has been established by several authors (see Table V). Lepomis humilis died within one hour in a concentration of 61-65 ppm toluene. Preceding death, behavioral abnormalities such as erratic movement, intoxication, and leaping out of the tank were noted (88). Toluene sensitivities were tested by Pickering and Henderson (1966) for a number of

TABLE V

REPORTED TOLUENE TOXICITY TO AQUATIC ANIMALS

	Concentration (ppm) Resulting in Death of All Organisms within 2 Hours	Reported TL_{50} Values (ppm)			Reference
		24 Hours	48 Hours	96 Hours	
Pimphales promelas (fathead minnow)	--	46.31	46.31	34.27	89
Lepomis macrochirus (bluegill)	--	24.00	24.0	24.0	89
Carassius auritus (goldfish)	--	57.68	57.68	57.68	89
Lebistes reticulatus (guppies)	--	62.81	60.95	59.30	89
Lepomis humilis (orange-spotted sunfish)	61-65	--	--	--	88

Adapted from: Assessing Potential Ocean Pollutants, National Academy of Sciences, Washington, D. C. 1975.

fresh-water fish. Bluegills (Lepomis macrochirus) were most susceptible to poisoning, reacting at 24 ppm. Goldfish (Carassius auratus) and guppies (Lebistes reticulatus) exhibited almost identical sensitivities to the toxicity of toluene, responding to 57-62 ppm, while fathead minnows (Pimephales promelas) were affected at 34-46 ppm. Soft water was found to increase toluene's toxicity to the minnows by almost 10 ppm and a slight difference in TL_{50}* values during 24- and 96-hour exposures occurred (89).

*The concentration that will kill 50 percent of a population in the specified time.

C. AMBIENT DATA, POPULATION AT RISK AND MEASUREMENT TECHNOLOGY

The estimated normal concentration of ambient toluene in urban samples is reported to be 0.01 to 0.05 ppm (90). This level is not based on a vast compilation of data since toluene, as an entity, is not routinely monitored as ambient air. In response to complaints during 1974, the OSHA analyzed 1867 industrial atmospheric samples for toluene. However, a summary of the resultant levels detected is not readily available (91, 92).

One report of the evaluation of atmospheric benzene and toluene levels was based on continuous sampling for nine days at 17 sampling stations in Toronto, Canada. Quantitation of toluene revealed a maximum concentration of 188 ppb with an average concentration of 30 ppb. Based upon three factors, it was concluded that the toluene contamination of the air was linked to automotive transportation. The three key factors for this conclusion were: 1) the ratio of toluene to benzene; 2) the presence of distinct maxima for both hydrocarbons at 0700, 1500, and 2100 hours; and 3) the relative concentrations detected at various sampling stations (93).

Analysis of aromatic hydrocarbons in Los Angeles in 1966 revealed an 0.11 ppm average concentration for total aromatics (94). Toluene was the most abundant constituent with an average concentration of 37 ppb. This value was approximated once again in 1967. Los Angeles air was quantitated to contain an average 30 ppb toluene while suburban Azusa had only half the Los Angeles value (95).

Several reports of industrially-measured toluene were found in the literature. As recently as 1967, levels of toluene were quantitated to be 10,000 to 30,000 ppm due to inadequate ventilation in the hold of a merchant ship that was being internally sprayed with a toluene-containing insecticide (96). Two hours after the initial monitoring, a range of 5000 to 10,000 ppm was recorded. The hazard presented by these levels was not only potentially injurious to health but also constituted a fire (explosion) hazard. In 1969, the ambient toluene concentrations in 11 workshops of 8 factories operating polychromic rotary processes for photogravure printing were reported to range from 4 to 240 ppm (49).

Results released in 1971, relating a study initiated in 1953 in a rotogravure plant, reveal significant levels of toluene detected in the workroom air. From 1954 to 1956, concentrations varied from 0 to 240 ppm in various areas of the facility, while an annual mean of 203 ppm in the center of the room and near one of the folding machines and 431 ppm between the machine elements was tabulated from 1957 to 1965. In 1966, due to relocation of the plant and improved ventilation, the annual mean toluene concentration was 156 ppm near the folding machines and 265 ppm between the elements (38).

Atmospheric toluene concentrations cited herein reflect only the prevailing conditions at the time of the investigation, not peak exposure which may result from breakdown or leakage of equipment, transfer operations, or accidental spills.

Determination of the risk to the general population, not those employed in industries utilizing toluene, is difficult using the low environmental levels detected. If a cumulative effect exists, then the hazard may be significant. To estimate the risk generated by a production facility, a theoretical plant, releasing toluene through ventilation and exhaust of internal air, will be examined.

Atmospheric dispersion would distribute the gaseous emissions downwind, as affected by the turbulent diffusion of the air. Hypothetical plant conditions could be used as inputs to a Gaussian plume equation* from Turner's Workbook of Atmospheric Dispersion Estimates (97). The basic diffusion equation should be modified, however, due to the effect of the plant itself on the flow of air. Mechanical turbulence in the wake of a building tends to produce aerodynamic downwash, resulting in the fairly rapid diffusion of a gaseous emission

---

*Ground level downwind concentrations resulting from a point source are predicted by the following equation:

$$X(x, \ , 0; H) = \frac{Q}{\pi \sigma_y \sigma_z u} \exp\left[-1/2\left(\frac{H}{\sigma_z}\right)^2\right]$$

where: Q = uniform emission rate (grams/sec).
u = mean wind speed affecting the plume (meters/sec).
H = effective stack height, that is sum of stack height plus plume rise (meters).
σ_y = horizontal dispersion coefficient evaluated in terms of downwind distance to the point for which the concentration is being computed (meters).
σ_z = vertical dispersion coefficient evaluated in terms of downwind distance to the point for which the concentration is being computed (meters).
X = ground level concentration along plume axis (grams/meter^3).

down to the ground. This region of disturbed flow extends downwind, a distance equal to several times the height of the building. While this situation does not result in a Gaussian-distributed plume, it is proposed that a modification of the usual formula can be employed. This is because the turbulent mixing in the wake of the building is assumed to be distributed uniformly in the vertical direction, analogous to the situation there, a plume is trapped below an inversion layer. A limited vertical mixing height can be modeled, using the equation:

$$X(x,0,0;H) = \frac{Q}{\pi\sigma_y u\ (.8L)}$$

where L is the limit of the mixing depth. In the case of an isolated rectangular building it is assumed that L equals 1.5 times the building height.

In addition there is a horizontal wind turbulence which is assumed to result in an initial horizontal plume spread equal to the width of the building normal to the wind direction. This is analogous to an area source emission where the area equals the building top. This can be modeled using a further modification of the basic Gaussian diffusion equation. A virtual point source is assumed upwind from the building at a distance where the plume spread (for the given stability conditions) would equal the crosswind width of the building. The modified diffusion equation is therefore:

$$X(x,0,0;H) = \frac{Q}{\pi\sigma'_y u\ (1.2h)}$$

where h is the building height and σ'_y is based on the downwind distance to the receptor point plus the upwind distance to the virtual point source.

Generally speaking, toluene production from petroleum feedstocks is conducted in out-of-doors facilities with pressure-tight reaction and separation vessels. Thus, atmospheric release would be virtually nonexistent. However, as a most conservative approximation, assume that a hypothetical plant produces 160 million gallons of toluene annually, operating 360 days a year, 24 hours a day. Also assume that ten percent of this yield is lost in the form of flue gases, which are then treated by an emission control technique having a 98 percent efficiency. Additionally, assume that the building height is 50 feet (15.24 meters) and its width is 100 feet (30.48 meters). In this hypothetical example, the ambient toluene concentration 500 meters downwind of the plant is estimated to be 2.3 mg/m^3 or 0.623 ppm.* A downwind distance of 500 meters was chosen to represent a point within the perimeter of the production facility. Ambient concentrations in surrounding neighborhoods could be expected to be significantly lower. An individual positioned at this location would immediately be exposed to a greater concentration of toluene than that reported to enhance brain electropotential, a concentration of 1.5 mg/m^3 (0.398 ppm) (32). The medical significance of this effect has not been reported, only that it is a predictable effect upon

*Additional assumption: (1) toluene is nonreactive; (2) the stability class is neutral; (3) the wind speed is 6 meters/second.

exposure to toluene at a concentration of 1.5 mg/m^3 (0.398 ppm). However, a person would have to remain at this same location for more than 275 days in order to inhale an amount equivalent to a worker exposed to the time-weighted average (100 ppm) during a 40-hour work week established by the NIOSH (55).

The danger of ambient toluene concentrations in relation to injury or disease is difficult to ascertain due to the lack of data correlating determined exposure levels with specific effects in the human population. If this situation were an actuality, it would be prudent to reduce the emissions, through use of controls and safety procedures, at least to the levels routinely found in urban areas. This reduction would not necessarily guarantee the safety of the surrounding population; however, it would ensure exposure levels comparable with those of the general populace. The primary risk associated with toluene would probably be to individuals employed by industries that utilize open system procedures during either the production of toluene or the use of the chemical as an intermediary. More information pertaining to industrial toluene vapor levels is needed. This can be facilitated by sample collection coupled with toluene determination.

Various methodologies for collection of air samples have developed. Both silica gel and activated charcoal have been used as adsorbents for toluene in room temperature air. A prefilter of molecular sieves is commonly used with silica gel to remove water vapor, as

moisture can have a damaging effect on the ability of silica gel to adsorb toluene (98). The use of activated charcoal can eliminate this problem since the affinity of water for activated charcoal (or carbon) is very low. Therefore, the use of activated charcoal, particularly in moist atmospheres, is recommended for the sampling of compounds that are weakly adsorbed on silica gel (99). A description of the design of activated charcoal tubes for sampling of toluene vapor in industrial atmospheres and the conditions of sampling and desorption has been prepared by White, et al. The charcoal tubes are reported to have averaged desorption efficiencies of greater than 97 percent for 100 ppm concentrations of toluene sampled alone, and of greater than 93 percent when sampled in the presence of six other organic vapors (90).

Other collection methods have included grab samples (100), bubblers (101), and absorption in scrubbers by nitrating solutions (102, 103). The use of plastic-film bags for collecting grab samples may result in loss of samples due to adsorption or permeation of the toluene vapor through the plastic. Absorption by scrubbing liquids is inconvenient for obtaining personal breathing-zone samples because several scrubbers must be connected in series in order to assure a high collection efficiency (55).

The concentration of toluene in an air sample, using a cold trap, followed by direct injection into a gas chromatograph, is the most sensitive collection technique. However, with this method, only

one sample is available for analysis, a distinct disadvantage. A charcoal or silica gel procedure followed by solvent extraction, in contrast, provides the analyst with the opportunity to aliquot the sample for repeated determinations, allowing replication and confirmation of experimental results.

Extraction and/or preconcentration techniques for the detection of toluene in air or water samples have varied considerably. Both liquids and solids have been utilized as concentration adsorbents. However, the sensitivity increase facilitated by these techniques is accompanied by a longer sample workup and processing time. Since increased handling of a sample increases the potential for losses, the addition of predeuterated toluene to the sample before processing would supply a valuable measurement (104). Establishment of the deuterated to undeuterated toluene ratio after concentration would allow a more accurate determination of the toluene contamination of the sample.

A continuous flow instrument has been devised for the determination of relative amounts of trace organics in chemical plant effluent based upon the ultraviolet adsorption of the aqueous solution. The light source used is a mercury discharge lamp (approximately 253.7 nm). This method is sensitive to 50 ppb toluene, but it is not specific for the hydrocarbon, since many other compounds also absorb ultraviolet light (105).

Direct analysis of air samples has also been reported. Gas chromatography with direct injection (3 ml samples) was used to analyze ambient toluene in both air samples and in synthetic photochemical "smogs." The sensitivity of a flame ionization (FI) detector was sufficient to detect individual aromatic hydrocarbons in the 0.05 to 1 ppm range in synthetic smog and in the 0.005 to 4 ppm range in ambient air samples (106, 107).

Other analytical methods for the detection of toluene include direct ultraviolet spectrophotometry (108, 109, 110), colorimetry which involves nitration followed by reaction with various ketones (101, 102, 110), gas chromatography (111, 112, 113, 114, 115), direct estimation by means of colorimetric indicator tubes based on the colorimetric reaction between toluene and formaldehyde in the presence of sulfuric acid (116, 117).

For the analysis of toluene samples, gas chromatography is believed to be the method of greatest specificity and sensitivity. A wide variety of compounds interfere with both the colorimetric and direct spectrophotometric methods of analysis, as discussed previously. Colorimetric indicator tubes should be used only as a detection technique, not as a quantitative procedure (55).

D. SOURCES

Toluene is commercially produced in the United States from both coal and petroleum; however, the majority of the product is petroleum-derived. At the beginning of 1975, total U.S. toluene production capacity was 1040.5 million gallons per year (118). In 1971, the contribution of two additional sources, coal-derived and byproduct production, accounted for only 4 to 5 percent of the total volume produced (see Table VI) (119). Table VII contains a listing of U.S. toluene producers, the location of their facilities and the production capabilities of these facilities. Figures 2 and 3 depict the geographic distribution and relative capacities of these facilities.

Although toluene is present in low concentrations in crude oil and in gasoline fractions resultant from thermal and catalytic cracking and thermal reforming, neither are used as sources for the isolation of toluene. The principal source of toluene in the United States is catalytic reforming, which is used to convert naphthenes and paraffins in low-octane naphtha to a high-octane gasoline component. Occasionally, reforming is used specifically to produce aromatic hydrocarbons for chemical use; however, the feedstock differs for the two (119). Without knowledge of the operating conditions and rates at which catalytic reforming equipment is used at individual refineries and without information pertaining to feedstock composition, it is impossible to accurately estimate the quantity of toluene contained

TABLE VI

TOLUENE PRODUCTION BY DERIVATIVE (1971)

	Millions of Gallons	Percent of Total
Petroleum-derived		
catalytic reformate	712-725	83-84%
pyrolysis gasoline	100	12%
By-Product		
styrene manufacture	22-35	2-3%
Coal-derived		
coke ovens	13	2%
tar distillers	-	-

Source: M.G. Erskine, Chemical Economics Handbook, Stanford Research Institute, Menlo Park, California, 1972.

TABLE VII

U.S. TOLUENE PRODUCTION CAPACITY (1975)

PRODUCER	LOCATION	CAPACITY[1] (millions of gallons)
American Petrofina, Inc.	Port Arthur, Texas	18.0
	Big Spring, Texas	10.0
Armco Steel Corp.	Middletown, Ohio	0.3
Ashland Oil, Inc.	Ashland, Kentucky	30.0
	North Tonawanda, New York	15.0
Atlantic Richfield Co.	Houston, Texas	36.0
	Wilmington, California	18.0
Bethlehem Steel Corp.	Bethlehem, Pennsylvania	1.0
	Lackawanna, New York	1.8
	Sparrows Point, Maryland	0.5
C F & I Steel Corp.	Pueblo, Colorado	0.6
The Charter Co.	Houston, Texas	16.0
Coastal States Gas Corp.	Corpus Christi, Texas	30.0
Commonwealth Oil Refining Co., Inc.	Penuelas, Puerto Rico	NA
Crown Central Petroleum Corp.	Pasadena, Texas	14.0
Dow Chemical, U.S.A.	Midland, Michigan	18.0
Exxon Corp.	Baytown, Texas	65.0
Foster Grant Co., Inc.	Baton Rouge, Louisiana	NA
Gulf Oil Corp.	Philadelphia, Pennsylvania	20.0
	Port Arthur, Texas	8.0
Interlake, Inc.	Toledo, Ohio	0.1
Jones & Laughlin Industries, Inc.	Aliquippa, Pennsylvania	2.0
Kerr-McGee Corp.	Corpus Christi, Texas	20.0
Marathon Oil Co.	Texas City, Texas	13.0
The Mead Corp.	Woodward, Alabama	0.4
Mobile Oil Corp.	Beaumont, Texas	70.0
Monsanto Co.	Chocolate Bayou, Texas	45.0
	Texas City, Texas	7.0
Northwest Industries, Inc.	Lone Star, Texas	0.1
Phillips Petroleum Co.	Sweeny, Texas	10.0
	Guayama, Puerto Rico	80.0
Republic Steel Corp.	Youngstown, Ohio	0.8
Shell Chemical Co.	Deer Park, Texas	50.0
Skelly Oil Co.	El Dorado, Kansas	12.0
Standard Oil Co. of California	El Segundo, California	20.0
	Pascagoula, Mississippi	NA
Standard Oil Co. (Indiana)	Texas City, Texas	160.0
The Standard Oil Co. (Ohio)	Marcus Hook, Pennsylvania	8.0
Sun Oil Co.	Marcus Hook, Pennsylvania	30.0
	Tulsa, Oklahoma	20.0
	Corpus Christi, Texas	24.0
Tenneco, Inc.	Chalmette, Louisiana	15.0
Texaco, Inc.	Port Arthur, Texas	NA
	Westville, New Jersey	30.0
Union Carbide Corp.	Seadrift, Texas	NA
	Taft, Louisiana	20.0
Union Oil Co. of California	Beaumont, Texas	46.0
	Lemont, Illinois	14.0
Union Pacific Corp.	Corpus Christi, Texas	15.0
United States Steel Corp.	Clairton, Pennsylvania	5.0
	Geneva, Utah	0.9
TOTAL		1040.5

NA - not available.

[1] As of January 1, 1975. Capacity for toluene made from petroleum can be readily increased if demand warrants. Not all units are currently operating. Some companies do not separate toluene from other aromatics.

Source: 1975 Directory of Chemical Producers, United States of America, Chemical Information Services, Stanford Institute, Menlo Park, California.

FIGURE 2
GEOGRAPHIC DISTRIBUTION AND RELATIVE CAPACITIES OF TOLUENE PRODUCTION FACILITIES

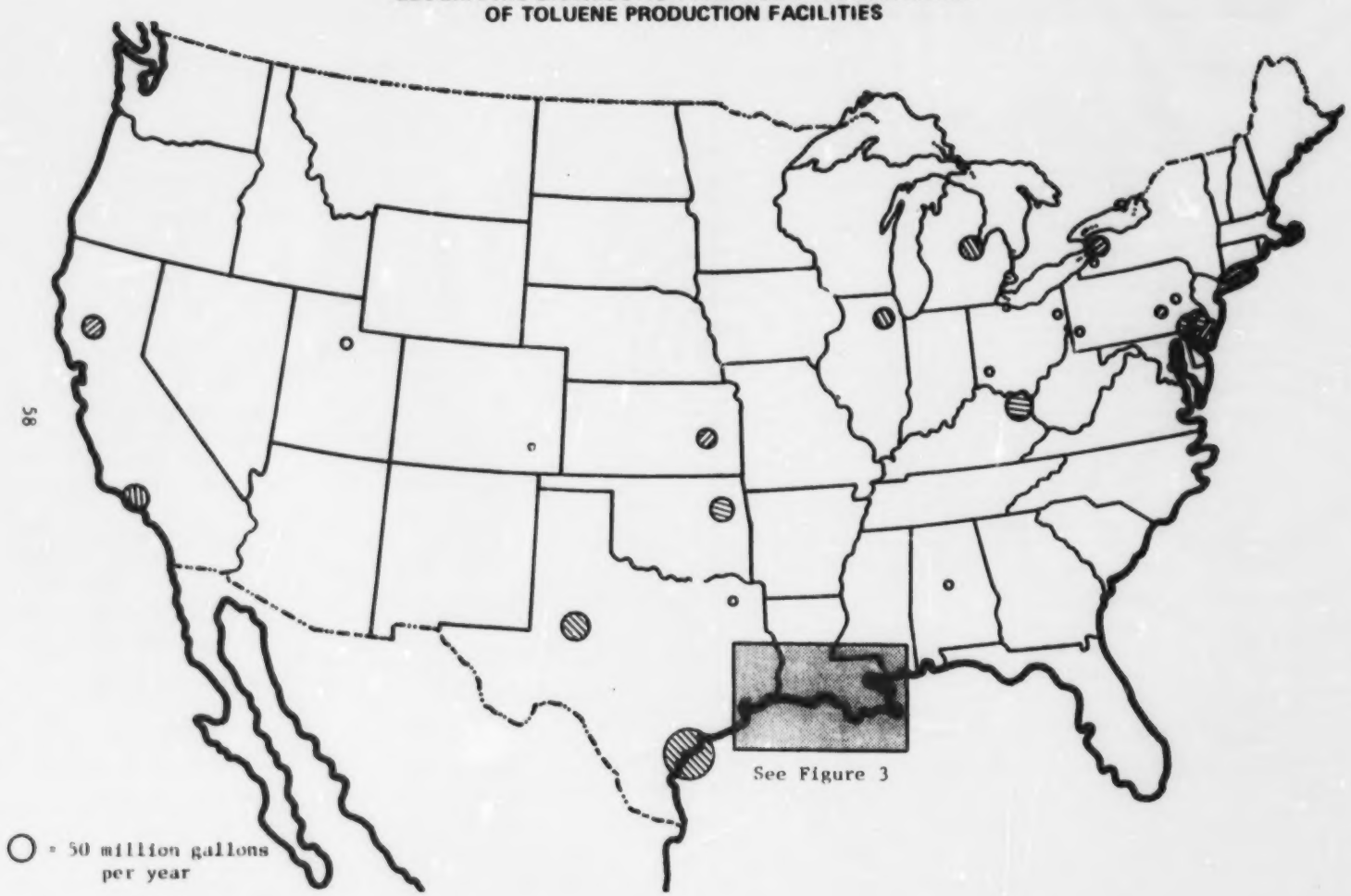
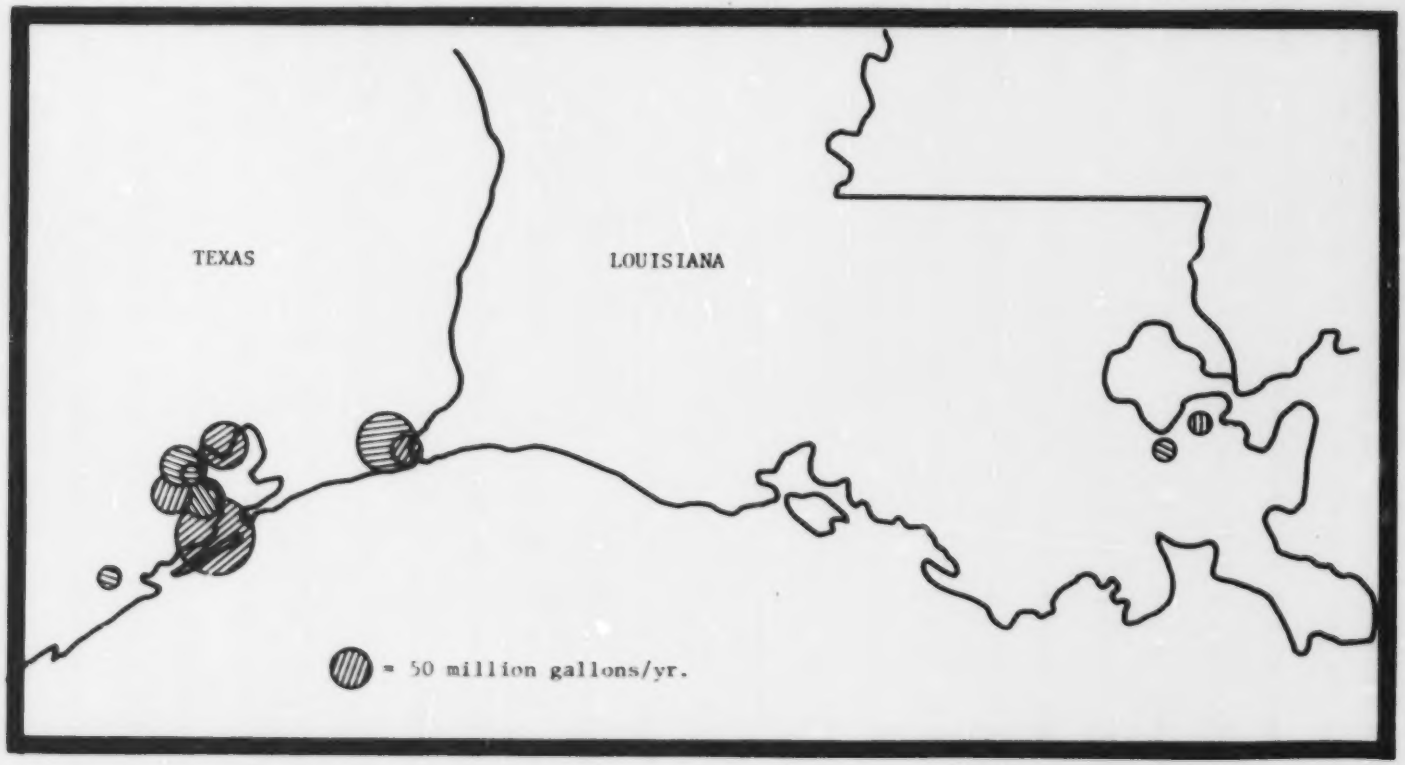


FIGURE 3
DISTRIBUTION AND RELATIVE CAPACITIES OF TOLUENE PRODUCTION FACILITIES ON THE TEXAS AND LOUISIANA COASTS



in catalytic reformate. The quantity potentially available from this source has been grossly estimated to far exceed any amount that will be required for the manufacture of chemicals in the future (119).

In January 1972, the catalytic reforming capabilities of the U.S. amounted to 3.2 million barrels per day or 45 billion gallons per year (120). If 45 billion gallons of straight run naphtha were fed to reforming, approximately 40 billion gallons of reformate containing 19 to 26 billion gallons of aromatics would result. Toluene would account for about 30 percent (the toluene content can fluctuate from 20 to 40 percent), or 6 to 9 billion gallons. Demand for toluene is only 10 to 15 percent of this amount.

The cracking of paraffins (i.e., propane and n-butane) or heavier hydrocarbons (i.e., condensates, naphtha, and gas oil) for the manufacture of olefins results in formation of pyrolysis gasoline as a byproduct. The quantity produced depends not only on the type of feed used, but on the conditions of cracking. Usually, the amount of the pyrolysis gasoline, which contains a high percentage of aromatics, coproduced with the olefins, is too small to make the recovery of toluene from it economically attractive (119). However, heavier feeds can yield substantial volumes of the pyrolysis gasoline and the quantity of toluene contained in the byproduct is generally dependent on the composition of the feedstock (see Table VIII). Not all of the pyrolysis gasoline produced in the United States is treated for toluene extraction, but some companies do isolate this toluene. In

TABLE VIII

TOLUENE CONTENT OF PYROLYSIS GASOLINE

Feed	Quantity of Toluene Produced per 100 Pounds of Ethylene	
	Gallons	Pounds
Gas Oil	1.5-3.5	11-25
Condensate	2-3	14-22
Naphtha	2-3	14-22

Source: M.G. Erskine, Chemical Economics Handbook, Stanford Research Institute, Menlo Park, California, 1972.

Europe, pyrolysis gasoline is a major source of aromatics; much of the pyrolysis gasoline produced by the U.S. is extracted. In 1971, it was estimated that 100 million gallons of toluene were reclaimed from pyrolysis gasoline, and that this source of toluene will become more significant as the availability of pyrolysis gasoline increases due to growing production of ethylene (119).

High-temperature carbonization of coal which produces coke also yields coal tar and crude light oil as byproducts, both of which contain toluene. The toluene is isolated from the crude light oil, but is seldom sought from the coal tar. Depending upon the type of coal used, the yield of light oil fluctuates from 2.5 to 3.4 gallons per ton of coal carbonized. On the average, three gallons of light oil, which contains 12 to 20 percent toluene by volume, are obtained for each ton of coal coked. This light oil may be processed by the coke-oven facilities or tar distillers for aromatics recovery or it may be sold to petroleum operators who use the oil as a supplementary feed for extraction of aromatics or for addition to gasoline (7, 119).

The quantity of toluene isolated from crude light oil by tar distillers and coke-oven operations is small. At one time, this source of toluene accounted for a significant proportion of the total production (i.e., in 1951, 50 percent of all the toluene produced was coal-derived), but in 1960, the quantity began to decline such that, by 1971, this source of toluene supplied less than two percent of total production. Petroleum refineries that process crude light oil

purchased from the coke-oven operators do so with the intent of increasing benzene production, not toluene. Some of the toluene is reclaimed, however, and in 1971 an estimated 15 to 20 million gallons of toluene were isolated by this process. It was also estimated that the relative value of light oil as a source of toluene will continue to decline but that the isolation of toluene from light oil will probably not cease completely (119).

One additional source of toluene is during the dehydrogenation of ethylbenzene to produce styrene. For each 100 million pounds of styrene produced, 0.5 to 0.8 million gallons of toluene are obtained. All of this byproduct toluene is reclaimed and used (i.e., for gasoline blending, feed for hydrodealkylation). In 1971 the production of styrene by this method totaled 4400 million pounds; therefore, the quantity of toluene realized may have been 22 to 35 million gallons (119).

Importation of toluene accounts for another source of toluene in the United States. The U.S. International Trade Commission reports that approximately 150,000 gallons of toluene, at a value of nearly $30,000, were imported in 1974. The bulk of this was obtained from Japan, Italy, Canada, and Netherland Antilles (121).

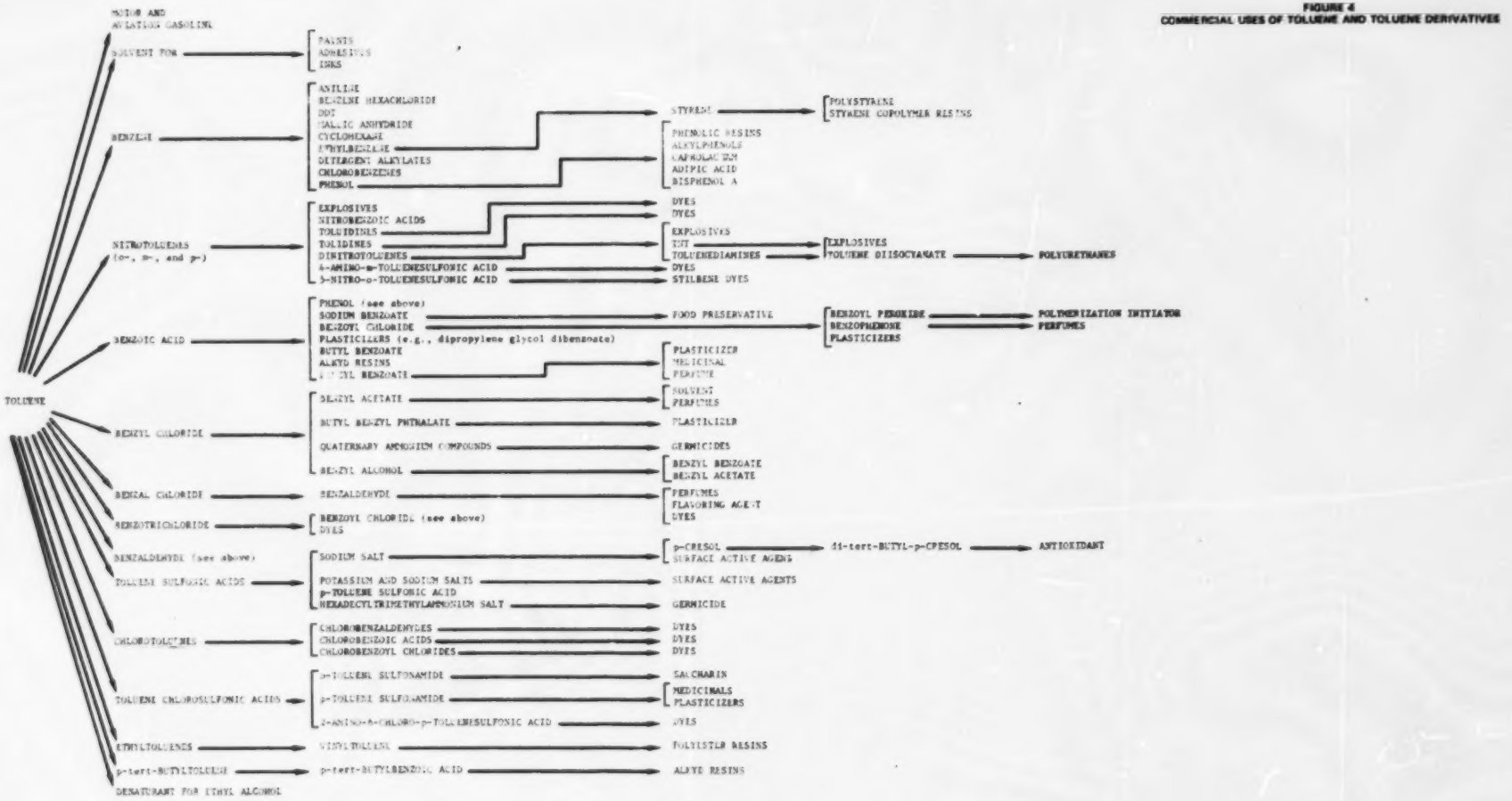
Benzene, toluene, and xylene (BTX) can also be extracted from the liquid byproduct of ethylene production by high severity pyrolysis. This mixture is stabilized by hydrotreating prior to the recovery of BTX aromatics by solvent extraction. The dissolved aromatics

are separated from the solvent (di- and triethylene glycol) by distillation, and the solvent-free aromatics are water-washed and then separated into benzene, toluene, and xylene. The separated solvent is regenerated and recycled to the process, while the sludge produced is disposed of in landfills or by combustion (122).

Toluene is normally contained in steel tanks and shipped in railroad tank cars, tank trucks, 55-gallon returnable or one-way metal drums, and barges (119). Due to its volatility, it is possible that some environmental contamination occurs during production storage and transport, although the Compilation of Air Pollution Emission Factors, published by the Environmental Protection Agency, states, "There are essentially no emissions from reforming operations," in the petroleum refining industry (123). The potential quantity lost is unknown; however, a reasonable assumption due to the economic incentive of the producer to limit losses, is that no more than one percent of the total is lost. This theoretical loss to the environment, based on the 1975 production capacity, would be approximately 10.4 million gallons dispersed in a relatively specific geographical area.

The major commercial application of toluene is as a component of motor and aviation fuel with use as a solvent and as an intermediate in the production of benzene consuming another large portion. Figure 4 is a compilation of all the possible commercial routes for toluene in the U.S., while Figure 5 illustrates the flow of toluene through

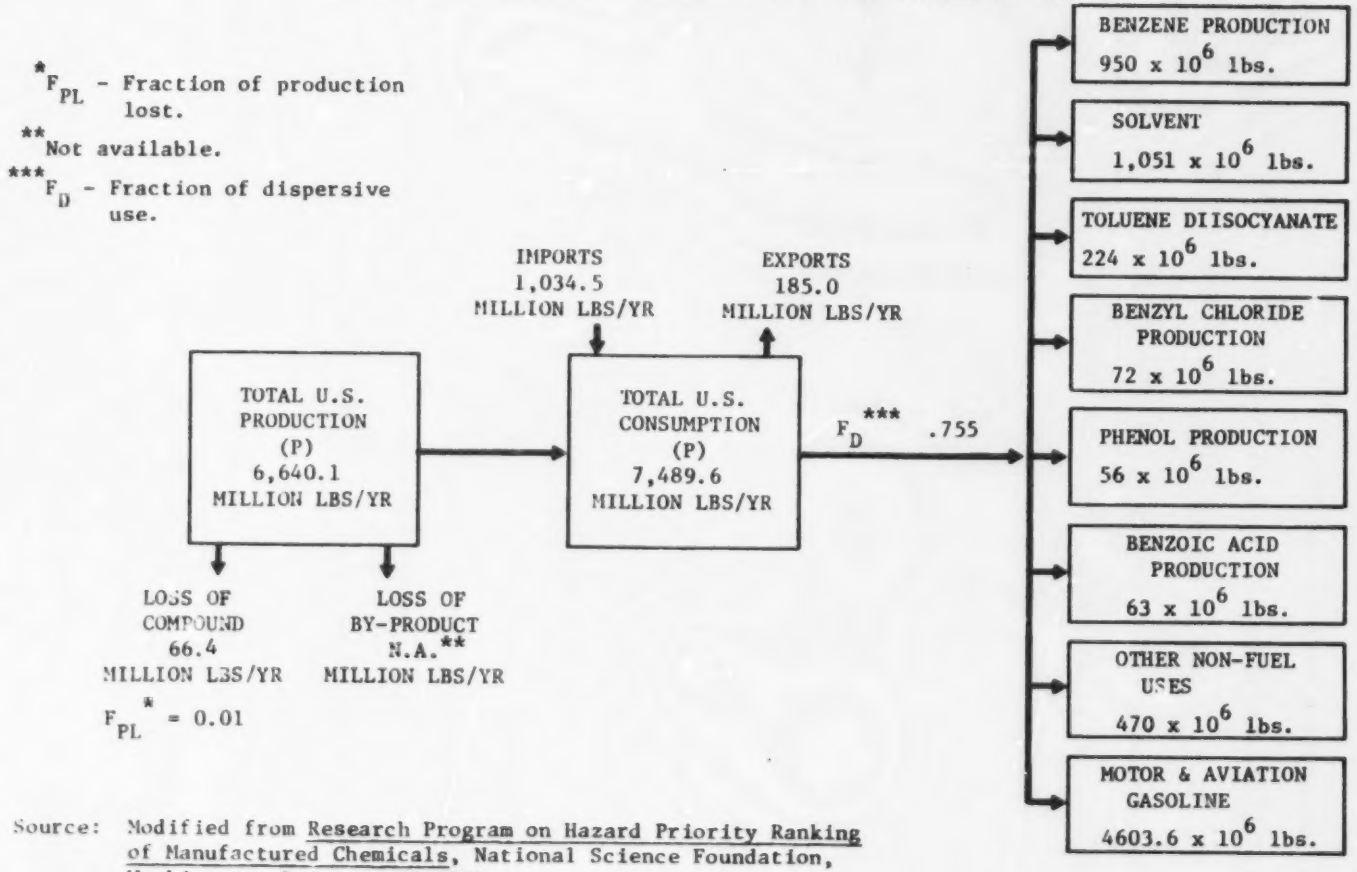
FIGURE 4
COMMERCIAL USES OF TOLUENE AND TOLUENE DERIVATIVES



Source: M. G. Erskine, Chemical Economics Handbook, Stanford Research Institute, Menlo Park, California, December 1972.

Preceding page blank

FIGURE 5
THE FLOW OF TOLUENE THROUGH THE UNITED STATES IN 1971



Source: Modified from Research Program on Hazard Priority Ranking of Manufactured Chemicals, National Science Foundation, Washington, D.C., April 1975.

the economy based on major uses (7, 119). Table IX lists the percentage of consumptive uses of toluene.

The efficiencies of the various methods of consumption fluctuate (119). If it is assumed that the difference between 100 percent and the reported yield is the amount of toluene potentially lost to the environment, the upper limit of loss is calculable (see Table X). These calculated losses are most likely much higher than those actually occurring due to the inclusion in the loss figure of quantities entering secondary synthetic steps rather than only those lost during the initial step involving toluene. In this calculation, toluene accounted for as lost may have actually been converted into a byproduct or recycled. Thus, the loss figures reflect a most conservative upper bound. The last category in Table X, "other nonfuel uses," includes the consumption of toluene for TNT, dinitrotoluene, toluene sulfonates, vinyl toluene, p-cresol, toluene diamine, and several other derivatives. The actual quantity in this "other nonfuel uses" category is determined by difference and the losses would fluctuate on the processes employed. This category only amounts to approximately six percent of the total nonfuel consumption; therefore, no attempt was made to calculate the loss.

As with losses incurred during production, losses during byproduct synthesis are not dispersed evenly. Table XI contains a compilation of the producers of two of the major toluene byproduct chemicals accompanied by geographical location of the facilities and toluene

TABLE IX

CONSUMPTION OF TOLUENE[1]

USE	PERCENT
Manufacture of Benzene	13.7
Manufacture of Solvents	15.2
Manufacture of Toluene Diisocyanate	3.2
Manufacture of Benzyl Chloride	0.8
Manufacture of Phenol	0.9
Manufacture of Benzoic Acid	1.1
Other Non-Fuel Uses	6.8
Motor and Aviation Gasoline Blending	58.3

[1] 1971 estimate.

Source: M.G. Erskine, Chemical Economics Handbook, Stanford Research Institute, Menlo Park, California, 1972.

TABLE X

UPPER LIMIT OF THE AMOUNT OF TOLUENE LOST FROM BY-PRODUCT MANUFACTURING FACILITIES IN 1971

Application	Consumption (10^6 lbs.)	100% Minus % Yield*	Amount of Toluene Unaccounted For (10^6 lbs.)
Benzene	950	4%	38
Solvent	1,051	100%	1051
Toluene Diisocyanate	224	24%	53.8
Benzyl Chloride	72	10%	7.2
Phenol	56	22%	12.3
Benzoic acid	63	10%	6.3
Other non-fuel uses	470	-	-
			1138.6

* The yields used are for overall yields to the various by-products. Some of these processes are more than one step and, therefore, the losses may be not only toluene but also the intermediate compounds. In the case of solvent usage it was assumed that 100% was lost to the environment during use.

Source: Data from M. G. Erskine, "Toluene," Chemical Economics Handbook, Stanford Research Institute, Menlo Park, California, December 1972.

TABLE XI

LOCATION AND TOLUENE USAGE CAPACITY OF FACILITIES
PRODUCING BENZOIC ACID AND TOLUENE DIISOCYANATE
FROM TOLUENE (1972)

Company and Location	Toluene Usage Capacity (10^6 Gals./Year)	
	Benzoic Acid	Toluene Diisocyanate
Allied Chemical Corporation Specialty Chemicals Division Moundsville, West Virginia		6.79
BASF Wyandotte Corporation Industrial Chemicals Group Geismar, Louisiana		8.73
Bagchem Corporation Mobay Chemical Company Division Cedar Bayou, Texas		9.70
New Martinsville, West Virginia		9.70
E.I. DuPont de Nemours & Co., Inc. Elastomer Chemicals Department Deepwater Point, New Jersey		16.49
Kalama Chemical, Inc. Kalama, Washington	13.92	
Monsanto Company Monsanto Industrial Chemicals Co. St. Louis, Missouri	1.16	
Northwest Industries, Inc. Velsicol Chemical Corp., Subsidiary Chattanooga, Tennessee	6.96	
Olin Corporation Chemicals Group Ashtabula, Ohio		3.88
Lake Charles, Louisiana		8.73
Pfizer, Inc. Chemicals Division Terre Haute, Indiana	1	

TABLE XI (Continued)

Company and Location	Toluene Usage Capacity (10^6 Gals./Year	
	Benzoic Acid	Toluene Diisocyanate
Rubican Chemicals, Inc. Geismar, Louisiana		3.40
Tenneco, Inc. Tenneco Chemicals, Inc. Tenneco Intermediates Division Garfield, New Jersey	13.92	
Union Carbide Corporation Chemicals and Plastics Division Institute, West Virginia		5.34

Source: M. G. Erskine, Chemical Economics Handbook, Stanford Research Institute, Menlo Park, California, December 1972.

consumption capacity. Comparison of Table VII with Table XI indicates the byproduct facility locations to be primarily southeast while many of the producers of toluene are located in the Northeast and Gulf Coast areas. Therefore, any significantly large loss during transport could occur along transportation routes between the Southeast and Northeast or Gulf Coast. The collision rate for tank cars has been calculated to be 1.52 collisions/10^6 miles (124); however, the quantity of toluene released in this manner is unknown.

Two significant sources of toluene contamination, not resulting from either commercial production or use, are oil spills and emissions from motor vehicles. The total oil influx into the ocean has been estimated to be 11 to 12,000 million pounds per year. This contamination arises from routine tanker discharges, accidents both in port and in free waters, during oceanic exploration and production, from pipeline breakage, discarded lubricants, incompletely burned fuel and from untreated industrial and domestic sewage (125). The toluene content of crude oil reportedly fluctuates from 1.19 percent to 1.39 percent (126). Assuming an average toluene concentration of 1.3 percent by weight in crude oil, between 143 and 156 million pounds of toluene are annually released into the oceans and waterways.

The contamination of the environment due to the toluene content of motor vehicle exhaust is more difficult to estimate. Both fuel evaporation and exhaust emissions are potential appreciable sources of loss. In terms of grams per vehicle mile for passenger vehicles,

approximately 20 percent of the transportation hydrocarbon emissions in an urban location are due to evaporation with the remainder due to exhaust (127). The total hydrocarbon emissions from transportation sources was estimated to be 29,400 million pounds in 1971. This figure is approximately 55 percent of the total hydrocarbon emissions (128). The amount of toluene in fuel fluctuates from 8 to 10 percent with the grade used (129).

Toluene, one of the more volatile components of gasoline, increases and decreases in its relative proportion during evaporation, depending upon the volatilities of all the constituents of the fuel (130). If it is assumed that toluene consistently comprises nine percent of gasoline vapor and that gasoline vapor is 20 percent of the total annual vehicle emission, the toluene loss to the environment is 529.2 million pounds due to gasoline evaporation. Toluene is, by volume, 5.97 percent of the hydrocarbon emissions from a reciprocating engine (131). Because the lower molecular hydrocarbons comprise more than 50 percent of the hydrocarbon emissions, the percentage of toluene, by weight, would be approximately 12 percent. Therefore, the benzene emissions for 1971 from automotive exhaust would be 2822.4 million pounds. The addition of the losses due to gasoline evaporation and motor vehicle exhaust yields an approximate value of 3,350 million pounds, which would probably be geographically dispersed in direct proportion to population distribution.

Another possible source of environmental toluene contamination arises from the production of coke. According to the American Iron and Steel Institute Annual Statistical Report, 1974, 62,256,066 tons of coke were produced in 1974 (132). For each ton of coke produced, a yield of 3.2 gallons of light oil is realized, of which 0.45 gallons are toluene (133). Emissions of toluene from the coke ovens have not been reported (134, 135); however, emissions of hydrocarbon calculated as methane have been estimated for coke ovens with no emission controls (136). Assuming that the emitted hydrocarbons from coke ovens are of the same constitution as the light oil that is produced, and extrapolating the methane values to toluene, 0.48 pounds of toluene are emitted to the atmosphere for each ton of coke produced. Therefore, in 1974, approximately 29.8 million pounds of toluene were released to the air in the vicinity of coke ovens, which are located primarily in Alabama, Illinois, Indiana, Ohio, and Pennsylvania (137).

A summation of the toluene emissions from commercial production and use as well as from nonproduction sources is contained in Table XII. These are most likely the major routes of entry into the environment; however, there may be other significant sources. As an example, the other 45 percent of the nontransportation hydrocarbon emissions sources may contain considerable concentrations of toluene, particularly fossil fuel combustion processes. The quantities involved are unknown and, therefore, emissions are incalculable.

TABLE XII

TOLUENE EMISSIONS TO THE ENVIRONMENT

(10^6 Pounds)

Source	Location	Quantity	Media of Entry	Controllability
Commercial toluene production, storage and transport	Northeast Gulf Coast	65 (assumed 1% of total production)	Air Water	Point source, Non-ducted, Feasible
Commercial toluene usage	Southeast and Northeast primarily	1138.6 (based on reaction yields)	Air Water	Point and extended source. Non-ducted, Feasible except for solvent application.
Oil Spills	Oceans and Rivers	143-156	Water	Extended source Non-ducted, Infeasible
Motor Vehicle Emissions	Similar to Population Distribution	3350	Air	Extended source, Non-ducted, Difficult
Coke Ovens	Primarily North Central States and Alabama	29.8 (1974)	Air	Point source, Non-ducted, Difficult

E. CONTROL

The domestic production of toluene and its wide variety of uses results in the potential occupational exposure of 100,000 people (55). Toluene emissions can be controlled by using vapor condensation apparatus and installing local exhaust ventilation in major isolated process sections where toluene emissions occur. Of the industrial atmospheric samples analyzed in 1974, it is estimated that 10% revealed a violation of the recommended standard (92) which states that workers shall not be exposed to toluene at a concentration greater than 100 parts per million (ppm) in air (375 mg/m^3) determined as a time-weighted average exposure for an 8-hour workday with a ceiling of 200 ppm (750 mg/m^3) as determined by a sampling time of ten minutes (55).

Several methods are available to control toluene emissions from industrial sources:

a. Substitution of process materials or equipment. If substitution of process materials or equipment is operationally and economically acceptable, this approach can be up to 100 percent effective in reducing toluene vapor exposures in industry. However, before this control technique is applied, careful consideration must be given to the health hazards which may result from use of the new material.

b. Proper Maintenance of Condensation Apparatus. The scrubbers and separators which are part of the catalytic reforming

process which produces toluene from petroleum should be well maintained in order to eliminate the possibility of worker exposure to high levels of toluene resulting from leaks in the system, and to reduce the possibility of fire.

c. Process Ventilation and Process Location. Ventilation systems have several advantages over other control techniques. They are relatively inexpensive, easy to install and operate. For the control of toluene, spark-proof fans and systems can be designed and used to prevent the accumulation or recirculation of toluene in work areas. Processes involving toluene should be isolated from other work areas, and entry to those areas should be restricted.

d. Proper Handling, Transport and Good Housekeeping. The handling, transport, and storage of toluene all present air quality control problems. Loading facilities should be equipped with a loading arm with a vapor collection adaptor, pneumatic, hydraulic, or other mechanical means to force a vapor-tight seal between the adaptor and the hatch. When loading through other than hatches, all loading and vapor lines should be equipped with vapor tight connections which close automatically when disconnected. It is estimated that these precautions can reduce 55 to 60 percent of volatile organic emissions (such as toluene) from uncontrolled sources

gasoline marketing and other organic transfer operations (138, 139).

Reduction of toluene emissions due to oil spills can only be effected by good housekeeping practices. These might be encouraged, however, by the levying of strict fines to offenders. In order to similarly reduce the hydrocarbon content in the atmosphere due to gasoline usage, only properly maintained automobiles appear as a feasible control. As a result of the activated carbon cannisters currently installed on a motor vehicle crankcase, perhaps as the median model year of automobiles in use increases, the total emissions of toluene as a result of crankcase fuel volatilization will decrease. This argument is supported by several sources (139, 140). For individual vehicles, light-duty crankcase and evaporative hydrocarbon emissions decreased by approximately 97 percent from pre-1963 automobiles to post-1972 automobiles (139). It is reasonable to assume that a fraction of these emissions will be toluene, and its reduction will closely follow total hydrocarbon reductions. Furthermore, with a vehicle population, nonmethane hydrocarbon reductions of 63 percent from 1970 to 1980 are projected for a decrease in total automotive emission of about 72 percent for the same time period (140). Again, it is reasonable to assume that toluene emissions will closely track these overall figures.

Existing controls for coke oven operations are currently being expanded and updated. Controls for both the coke oven and larry car

are being investigated. The controls for the larry car consist of a totally enclosed environmentally controlled operator cabin, an automatic and sequential lid lifting mechanism, a drop sleeve chute providing a seal with a charging hole, remote control operation ability of gravity hopper coal feed systems, a positive seal over the discharge hole, and a remote alignment system operation. Controls for the coke oven include a steam ejector or aspirating system to provide negative pressure within the oven during charging, improved lids having a modified design mating with an automatic mechanism on the larry car, and a double gas off-take relief piping to alleviate possible internal pressures caused by coal-oven roof blockage (141).

Table X contains a summary of the primary sources of toluene emissions and the feasibility of control for each. A ducted (having a stack) point source will be the method of dispersion with the greatest feasibility of control while the nonducted extended sources can be contained only by proper handling and operation techniques and adequate maintenance of the system involved.

REFERENCES

1. National Science Foundation Research Program on Hazard Priority Ranking of Manufactured Chemicals, SRI Project ECU-3386, April 1975.

2. "Manufacturing Chemists' Association: Chemical Safety Data Sheet SD-63 Toluene," Manufacturing Chemists Assoc., Washington, D.C., 18, 1956.

3. R. C. Weast, ed., Handbook of Chemistry and Physics, ed. 52, The Chemical Rubber Co., Cleveland, Ohio, 1971.

4. Assessing Potential Ocean Pollutants, National Academy of Sciences, Washington, D.C., 133-135, 1975.

5. D. W. Fassett and D. I. Irish, eds., Industrial Hygiene and Toxicology, Second Revised Edition, Volume II, Toxicology, Interscience, New York, 1222-1229, 1963.

6. Stanford Research Institute, "Research Program on Hazard Priority Ranking of Manufactured Chemicals," SRI Project, ECU-3386, April 1975.

7. M. G. Erskine, Chemical Economics Handbook, Organic Chemicals P-Z, 696.503D, Stanford Research Institute, Menlo Park, California, 1967.

8. "Azeotropic Data," Advan. Chem Ser 6, 1952.

9. Kirk and Othmer, eds., The Encyclopedia of Chemical Technology, Vol. 20, 527-565, 1964.

10. L. Selling, "Benzol as a Leucotoxin--Studies on the degeneration and regeneration of the blood and the hemopoietic system" (in German). Beitr. Pathol. Anat., 54, 576-579, 1911.

11. T. Ferguson, W. F. Harvey, and T. D. Hamilton, "An enquiry into the relative toxicity of benzene and toluene," J. Hyg., 33, 547-575, 1933.

12. J. J. Batchelor, "The relative toxicity of benzene and its higher homologues," Am. J. Hyg., I, 276-298, 1927.

13. R. Kowal-Gierczak, K. Kuczynska-Sekieta, A. Cieslinska, M. Wrzyszcz, and J. Malolepszy, "Some biochemical tests in subjects with chronic toluene exposure," (in Polish), Pol. Tyg. Lek., 24, 1682-1685, 1969.

14. A. Cieslinska, B. Kowal-Gierczak, K. Kuczynska-Sekieta, J. Malolepszy, and M. Wrzyszcz, "Serum iron and copper levels in subjects with chronic toluene exposure," (in Polish), Pol Tyg. Lek., 24, 1848-1850, 1969.

15. Manufacturing Chemists' Association. "Chemical Safety Data Sheet SD-63 Toluene," Manuf. Chemists' Association, Washington, D.C., 18, 1956.

16. W. Banfer, "Studies on the effect of pure toluene on the blood picture of photogravure printers and helper workers," (in German), Zentralbl. Arbeitsmed., 11, 35-40, 1961.

17. E. Browning, Toxicity and Metabolism of Industrial Solvents, Elsevier Publishing Co., New York, 66-76, 1965.

18. A. Chassevant, M. Garnier, "The toxicity of benzene and some aromatic hydrocarbon homologs," (in French), C.R. Soc. Biol., 55, 1255-1257, 1903.

19. M. P. Francone and L. Braier, "The basis for the substitution of benzene by the higher homologs in industry," (in Italian), Med. Lavoro, 45, 29-32, 1954.

20. H. W. Gerarde, Toxicology and Biochemistry of Aromatic Hydrocarbons, Elsevier Pub. Co., New York, 141-150, 1960.

21. T. Dutkiewicz and H. Tyras, "The quantitative estimation of toluene skin absorption in man," Arch. Gewerbepath. Gewerbehyg., 24, 253-257, 1968

22. J. Piotrowski, "Quantitative estimate of the absorption of toluene in people," (in Polish), Med. Pracy., 18, 213-223, 1967.

23. A. Capellini and L. Alessio, "The urinary excretion of hippuric acid in workers exposed to toluene," (in Italian), Med. Lavoro., 62, 196-201, 1971.

24. C. P. Carpenter, C. B. Shaffer, C. S. Weil, and H. F. Smyth, Jr., "Studies on the inhalation of 1,3-butadiene; with a comparison of its narcotic effect with benzol, toluol, and styrene, and a note on the elimination of styrene by the human," J. Ind. Hyg. Toxicol., 26, 69-78, 1944.

25. R. S. McLaughlin, "Chemical burns of the human cornea," Am. J. Opthalmol., 29, 1355-1362, 1946.

26. W. M. Grant, Toxicology of the Eye, Charles C. Thomas, Springfield, Illinois, 544-545, 1962.

27. W. F. von Oettingen, P. A. Neal, and D. D. Donahue, The toxicity and potential dangers of toluene--preliminary report," J.A.M.A. 118, 579-584, 1942.

28. W. F. von Oettingen, P. A. Neal, D. D. Donahue, J. L. Svirbely, H. D. Baernstein, A. R. Monaco, P. J. Valaer, and J. L. Mitchell, "The toxicity and potential dangers of toluene with special reference to its maximal permissible concentration," Public Health Service Bulletin 279, 50, 1942.

29. R. H. Wilson, "Toluene poisoning," J.A.M.A., 123, 1106-1108, 1943.

30. R. Satran and V. N. Dodson, "Toluene habituation--report of a case," N. Eng. J. Med., 268, 719-721, 1963.

31. J. W. Knox and J. R. Nelson, "Permanent encephalopathy from toluene inhalation," N. Eng. J. Med., 275, 1494-1496, 1966.

32. I. S. Gusev, "Comparative toxicity studies of benzene, toluol, and xylol by the reflex activity method," in The Biological Effects and Hygenic Importance of Atmospheric Pollutants, Book 10, Literature on Air Pollution Occupational Diseases, Vol. 17, 60-67, 1968.

33. I. S. Gusev, "Reflective effects of microconcentrations of benzene, toluene, xylene and their comparative assessment," Hyg. Sanit., 30(12), 331-336, December 1965.

34. E. T. O'Brien, W. B. Yeoman, and J. A. E. Hobby, "Hepatorenal damage from toluene in a glue sniffer," Br. Med. J., 2, 29-30, 1971.

35. L. Greenburg, M. R. Mayers, H. Heimann, and S. Moskowitz, "The effects of exposure to toluene in industry," J.A.M.A., 118, 573-578, 1942.

36. I. Pacseri and G. Emszt, "Medical aspects of the exposure to toluol," (in Hungarian), Munkavedelem, 16, 41-46, 1970.

37. J. Bansagi, "Effect of toluene on the phagocytic activity of white blood cells in printers," (in Hungarian), Mundavedelem, 14, 26-28, 1968.

38. A. Forni, E. Pacifico, and A. Limonta, "Chromosome studies in workers exposed to benzene or toluene or both," Arch. Environ. Health, 22, 373-378, 1971.

39. L. Parmeggiani and C. Sassi, "Occupational risk of toluene: environmental studies and clinical investigations of chronic intoxication," (in Italian), Med. Lavoro, 45, 574-583, 1954.

40. R. Fabre, R. Truhart, S. Laham, and M. Peron, "Toxicological research on substitute solvents for benzene--II. Study of Toluene," (in French), Arch. Mal. Prof., 16, 197-215, 1955.

41. Y. Takeuchi, "Experimental studies on the toluene poisoning--chiefly on the findings of peripheral blood and adrenal gland," Ind. Health, 7, 31-45, 1969.

42. B. Speck and S. Moeschlin, "Effects of toluene, xylene, chloramphenicol, and thiouracil on bone marrow," (in German), Schweiz. Med. Wochenschr., 98, 1684-1686, 1968.

43. A. Sato, T. Nakajima, Y. Fujiwara, and K. Hirosawa, "Pharmacokinetics of benzene and toluene," Int. Arch. Arbeitsmed., 33(3), 169-182, 1974.

44. H. W. Gerard, "The aromatic hydrocarbons," in Industrial Hygiene and Toxicology, 2nd Rev., Volume II Toxicology, Interscience Publishers & Sons, Inc., New York, 1227-1229, 1963.

45. G. G. Fodor and M. Zimmerman, "Organic vapors. Occupational and general hazards of toluene vapors," (in German), Medizinisches Inst. fuer Lufthygiene und Silikoseforschung, 52-73, 1971.

46. M. Ogata, K. Tomokuni, and Y. Takatsuka, "Urinary excretion of hippuric acid and m- or p-methyl hippuric acid in the urine of persons exposed to vapors of toluene and m- or p-xylene as a text of exposure," Br. J. Ind. Med., 27, 43-50, 1970.

47. M. Ogata and K. Sugiyama, "Studies on the determination of urinary hippuric acid in toluene poisoning," (in Japanese), Japan J. Ind. Health, 4(5), 9-16, May 1962.

48. L. D. Pagnotto and L. M. Lieberman, "Urinary hippuric acid excretion as an index of toluene exposure," Am. Ind. Hyg. Assoc. J., 28, 129-134, 1967.

49. M. Ikeda and H. Ohtsuji, "Significance of urinary hippuric acid determination as an index of toluene exposure," Br. J. Ind. Med., 26, 244-246, 1969.

50. A. S. Faustov, "Change of relative toxicity in a homologous series of benzene derivatives related to the means of entrance into the organism," Tr. Voronezhsk. Med. Inst., 36, 243-243, 1960.

51. A. S. Faustov, "Toxicity of some aromatic hydrocarbons. I. Comparative toxicity of some aromatic hydrocarbons. II. Some problems of the toxic-hygienic properties of aromatic hydrocarbons," Tr. Voronezhsk. Med. Inst., 35, 247-255, 257-262, 1958.

52. Yu. Ye. Yakushevich, "Experimental data on hygienic assessment of continuous and intermittent action of benzene, toluol, and xylene," (in Russian), Gigiena I. Sanit., No. 4, 6-10, 1973.

53. H. F. Smyth and H. F. Smyth, Jr., "Inhalation experiments with certain lacquer solvents," J. Ind. Hyg., 10, 261-271, 1928.

54. J. L. Svirbely, R. C. Dunn, W. F. von Oettingen, "The acute toxicity of vapors of certain solvents containing appreciable amounts of benzene and toluene," J. Ind. Hyg. Toxicol., 25, 366-373, 1943.

55. National Institute for Occupational Safety and Health, U.S. Dept. of Health, Education and Welfare, Criteria for a Recommended Standard...Occupational Exposure to Toluene, 1973.

56. O. A. Pankovets, "Nonspecific reactions of an organism during poisoning with aromatic hydrocarbons," Tr. Voronezhsk Lps. Med. Inst., 73(4), 47-52, 1968.

57. I. Mizoguchi, M. Osawa, Y. Sato, K. Makino, and H. Yagyu, "Studies on erythrocyte and photochemical smog, Part I: Effects of air pollutants on erythrocyte resistance," (in Japanese), J. Japan. Soc. Air Poilution, 8(3), 414, October 1973.

58. H. W. Gerarde, "Toxicological studies on hydrocarbons--II. A comparative study of the effects of benzene and certain mono-n-albylbenzenes on hemapoiesis and bone marrow metabolism in rats," AMA Arch. Ind. Health, 13, 468-474, 1956.

59. A. A. Lyapkalo, "Genetic activity of benzene and toluene," Gig. Jr. Prof. Zabol., 3, 1973.

60. V. B. Dobrokhotov, "Mutagenic action of benzene and toluene under experimental conditions," Gig. Sanit., 10, 36-39, 1972.

61. B. Speck and S. Moeschlin, "Effects of toluene, xylene, chloramphenicol, and thiouracilon bone marrow," (in German), Schweiz. Med. Wochenschr., 98, 1684-1686, 1968.

62. A. S Faustov, "Standardization of toluene values in factory air," Hyg. Sanit., 32(7-9), 448-451, July-September 1967.

63. G. P. Babanov, Yu. A. Gurov, N. A. Skobei, L. G. Verkhovskii, G. G. Abramyan, I. A. Troitskaya, and A. L. Isakhamov, "Disadaptation symptons under the periodic effect of peak concentrations of toluene," Toksicol. Gig. Prod. Neftekhim, Proizvod., 32-45, 1972.

64. G. P. Babanov and Yu. A. Gurov, "Adaptation during the action of low concentration toxic factors on the body in industrial environments," (in Russian), Gigiena. I. Sanit., 37(1), 93-93, 1972.

65. M. A. Wolf, V. K. Rowe, D. D. McCollister, R. L. Hollingsworth, and F. Oyen, "Toxicological studies of certain alkylated benzenes and benzene," A.M.A. Arch. Ind. Health, 14, 387-398, 1956.

66. M. A. Wolf, et al., AMA Asch Ind Hlth, 14, 387-398, 1956.

67. W. E. Poel, N.C.I. Monograph, 10, 611-631, 1963.

68. J. V. Frei and W. F. Kingsley, J. Nat. Cancer Inst., 41:6, 1307-1313, 1968.

69. M. Ogata, T. Saeki, "The quantitation method for the toluene content in the blood using gas chromatography with a carburetor," (preprint in Japanese), Japan Soc. Ind. Hyg., 386-387, 1973.

70. O. M. Bakke and R. R. Scheline, "Hydroxylation of aromatic hydrocarbons in the rat," Toxicol. Appl. Pharmacol., 16, 691-700, 1970.

71. H. W. Gerarde, Toxicology and Biochemistry of Aromatic Hydrocarbons, Elsevier Pub. Co., New York, 141-150, 1960.

72. M. M. Abou-el-Makarem, P. Millburn, R. L. Smith, and R. T. Williams, "Biliary excretion of foreign compounds--benzene and its derivatives in the rat," Biochem. J., 105, 1269-1274, 1967.

73. M. Ikeda and H. Ohtsuji, "Phenobarbital--induced protection against toxicity of toluene and benzene in the rat," Toxicol. Appl. Pharmacol., 20, 30-43, 1971.

74. W. J. North, K. A. Clendenning, and H. L. Scotten, "The effects of waste discharges upon kelp," Institute of Marine Resources, University of California, La Jolla, California, 1959.

75. H. B. Currier, "Herbicidal properties of benzene and certain methyl derivatives," Hilgardia, 20, 383, 1951.

76. G. Bringmann and R. Kuhn, "The toxic effects of waste water on aquatic bacteria, algae, and small crustaceans," Gesundheits-Ing., 80, 115, 1959.

77. C. L. Woldringh, "Effects of toluene and phenethyl alcohol on the ultrastructure of Escherichia coli," J. Bacteriol., 114, 1973.

78. R. W. Jackson and J. A. DeMoss, "Effects of toluene on Escherichia coli," J. Bacteriol., 90(5), 1420-1425, 1965.

79. S. H. Howell and L. L. Walker, "Synthesis of DNA in toluene-treated Chlamydomonas," Proc. Nat. Acad, Sci. USA, 69, 1972.

80. K. Vas, "Mechanism of antimicrobial action interference with the cytoplasmic membrane," Agrokemia Es Talajtan, 2, 1953.

81. T. H. Sabalitschka and J. Preuss, "Action of toluene on bacteria," Deut. Apoth.-Ztg. Ver. Suddeut. Apoth-ztg., 94, 1954.

82. J. C. Buzzell, Jr., R. H. F. Young, and D. W. Ryckman, "Behavior of organic chemicals in the aquatic environment. II. Behavior in dilute systems," Manufacturing Chemists' Association, Washington, D.C., 1968.

83. F. Kapralek, "Assimilation of hydrocarbons by microorganisms," Ceskoslov. Biol., 3, 82-91, 1954.

84. D. Claus and N. Walker, 'The decomposition of toluene by soil bacteria," J. Gen. Microbiol., 36, 107-122, 1964.

85. D. T. Gibson and W. K. Yeh, "Microbial degradation of oil pollutants workshop, December 4-6, 1972, Georgia State University, 33-38, 1972.

86. D. T. Gibson, "Initial reactions in the degradation of aromatic hydrocarbons," in Degradation of synthetic organic molecules in the biosphere: Natural, pesticidal and various other man-made compounds, National Academy of Sciences, Washington, D.C., 116-136, 1972.

87. R. F. Lee, R. Sauerherer and A. A. Benson, "Petroleum hydrocarbons. Uptake and discharge by the marine mussel Mytilus edulis," Science, 177, 344-346, 1972.

88. V. E. Shelford, "An experimental study of the effects of gas waste upon fishes with especial reference to stream pollution," Bull. Ill. Lab. Nat. Hist., 11, 381-412, 1917.

89. Q. H. Pickering and C. Henderson, "Acute toxicity of some important petrochemicals to fish," J. Water Pollut. Control Red., 38, 1419-1429, 1966.

90. A. P. Altshuller, Atmosphere Analysis by Gas Chromatography, U.S. Dept. of Health, Education, and Welfare, Public Health Service, Division of Air Pollution, 1969, and California Dept. of Public Health, SDPH1-SDPH1-50, August 1966.

91. Dr. Russell Heinricks, personal communication, August 1975.

32. Floyd Madsen, personal communication, August, 1975.

93. S. Pilar, W. F. Graydon, "Benzene and toluene distribution in Toronto atmosphere," Environmental Science & Technology, 7/7, 628-631, July 1973.

94. W. A. Lonneman, T. A. Bellar, and A. P. Altshuller, Aromatic hydrocarbons in the atmosphere of the Los Angeles Basin," Environ. Sci. Technol., 2, 1017-1020, 1968.

95. A. P. Altshuller, S. L. Kopczynski, W. A. Lonneman, F. D. Sutterfield, and D. L. Wilson, "Hydrocarbon composition of the atmosphere of the Los Angeles Basin, 1967," Environ. Sci. Technol., 5, 1009-1016, 1971.

96. E. O. Longley, A. T. Jones, R. Welch, and O. Lomaev, "Two acute toluene episodes in merchant ships," Asch. Environ. Hlth., 14, 481-487, 1967.

97. D. B. Turner, Workbook of Atmospheric Dispersion Estimates, U.S. Department of Health, Education, and Welfare, Revised 1969.

98. N. E. Whitman and A. E. Johnston, "Sampling and analysis of aromatic hydrocarbon vapors in air: A gas-liquid chromatographic method," Am. Ind. Hyg. Assoc. J. 25, 464-469, 1964.

99. H. Buchwald, "Activated silica gel as an adsorbent for atmospheric contaminants," Am. Ind. Hyg. Assoc. J. 31, 343-348, 1970.

100. B. S. Smith, J. O. Pierce, "The use of plastic bags for industrial air sampling," Am. Ind. Hyg. Assoc. J. 31, 343-348, 1970.

101. R. G. Bond, C. P. Straub, Handbook of Environmental Control, Volume I: Air Pollution, 108, 1972.

102. B. H. Dolin, "Determination of benzene: Detection and estimation of benzene in the presence of toluene, xylene, and other substances," Ind. Eng. Chem. Anal. Ed. 15, 242-247, 1943.

103. B. S. Levine (ed.), "Quantitative determination of benzene in the air," USSR Literature on Air Pollution and Related Occupational Diseases 8, 47-51, 1963.

104. S. P. Wasik, W. Tsand, "Determination of trace amounts of contaminants in water by isotope dilution gas chromatography," Anal. Chem., 42, 13, 1649-1651, 1970.

105. H. C. Bramer, M. J. Walsh, and S. C. Caruso, "Instrument for monitoring trace organic compounds in water," Water Sewage Works, 113, 8, 275-278, 1966.

106. A. P. Altshuller, T. A. Bellar, "Gas Chromatographic Analysis of Hydrocarbons in the Los Angeles Atmosphere," J. Air Pollution Control Assoc., 13, 2, 81-87, 1963.

107. A. P. Altshuller and C. A. Clemons, "Gas chromatographic analysis of aromatic hydrocarbons at atmospheric concentrations using flame ionization detection," Anal. Chem., 34, 466, 1962.

108. H. B. Elkins, L. D. Pagnotto, E. M. Comproni, "The ultraviolet spectrophotometric determination of benzene in air samples adsorbed on silica gel," Anal. Chem. 34, 1797-1801, 1962.

109. P. A. Maffett, T. F. Doherty, and J. L. Monkman, "A direct method for the collection and determination of micro amounts of benzene or toluene in air," Am. Ind. Hyg. Assoc. Quate. 17, 186-188, 1956.

110. Analytical Abstracts Committee, Analytical Abstracts, Benzene, American Industrial Hygiene Association, 1965.

111. C. L. Fraust, E. R. Hermann, "Charcoal sampling tubes for organic vapor analysis by gas chromatography," Am. Ind. Hyg. Assoc. J. 27, 68-74, 1966.

112. F. H. Reid, W. R. Halpin, "Determination of halogenated and aromatic hydrocarbons in air by charcoal tube and gas chromatography," Am. Ind. Hyg. Assoc. J. 29, 390-396, 1968.

113. R. J. Sherwood, F. W. G. Carter, "The measurement of occupational exposure to benzene vapor," Ann. Occup. Hyg. 13, 125-146, 1970.

114. R. Levadie, J. F. Harwood, "An application of gas chromatography to analysis of solvent vapors in industrial air," Am. Ind. Hyg. Assoc. J. 21, 20-24, 1960.

115. N. E. Whitman, A. E. Johnston, "Sampling and analysis of aromatic hydrocarbon vapors in air: A gas-liquid chromatographic method," Am. Ind. Hyg. Assoc. J. 25, 464-469, 1964.

116. P. Kaljkowsky, "Indicator-tube method for the determination of benzene in air," Analyst 94, 918-920, 1969.

117. R. M. Ash, J. R. Lynch, "The evaluation of gas detector tube systems--Benzene," Am. Ind. Hyg. Assoc. J. 32, 410-411, 1971.

118. Chemical Information Services, Stanford Research Institute 1975 Directory of Chemical Producers--U.S.A., 904-905.

119. M. G. Erskine, "Toluene," Chemical Economics Handbook, Stanford Research Institute, Menlo Park, California, December, 1972.

120. "Survey of Operating Refineries in the U.S.," Oil and Gas Journal, 136, March 7, 1972.

121. U.S. International Trade Commission, May 1975.

122. U.S. Environmental Protection Agency, Development Document for Proposed Effluent Limitations Guidelines and New Source Performance Standards for the Major Organic Products Segment of the Organic Chemicals Manufacturing Point Source Category, EPA 440/1-73/009, 82-85, December 1973.

123. Office of Air and Water Programs, U.S. Environmental Protection Agency, Compilation of Air Pollutant Emission Factors, 2nd edition, April 1973.

124. J. M. Lippian, "The transportation of hazardous materials: Transport of benzene by tank car," U.S. Nat. Tech. Inform. Serv., AD Rept. 771105, 1973.

125. M. Blumer, H. L. Sanders, J. F. Grassle, and J. R. Hampson, "A small oil spill," Environment, 13, 2, 2, 1971.

126. A. D. Green and C. E. Morrell, "Petroleum Chemicals," in Kirk-Othmer Encyclopedia of Chemical Technology, Vol. 10 1st Edit., Interscience Publ., Inc., N.Y., pp. 177-210, 1953.

127. R. E. Wendell, J. E. Norco, and K. G. Croke, "Emission prediction and control strategy: Evaluation of pollution from transportation systems," J. Air Pollut. Contr. Assoc., 23, 91, 1973.

128. Council on Environmental Quality, Environmental Quality--The Fourth Annual Report of the Council on Environmental Quality, P266, Government Printing Office, Washington, D.C., 1973.

129. W. N. Sanders and J. B. Maynard, "Capillary gas chromatographic method for determining the C_3-C_{12} hydrocarbons in full-range motor gasolines," Anal. Chem., 40, 3, 527-535, 1968.

130. B. J. Mair, "Hydrocarbons isolated from petroleum." Oil and Gas J., 62, 37, Sept. 14, 130-134, 1964.

131. K. Schofield, "Problems with flame ionization detectors in automotive exhaust hydrocarbon measurement," Environ. Sci. Technol., 8, 9, 826-834, 1974.

132. American Iron and Steel Institute, Annual Statistical Report, 1974, Washington, D.C., 1975.

133. W. L. Faith, D. B. Keyes, and R. L. Clark, Industrial Chemicals, 125-127, 1965.

134. Personal communication, Mr. Paul Caplan, Occupational Safety and Health Administration, Cincinnati, Ohio, November 1975.

135. Personal communication, Dr. Smith, Occupational Safety and Health Administration, Cincinnati, Ohio, November 1975.

136. U.S.E.P.A., Compilation of Air Pollution Emission Factors, RTP, North Carolina, 1973.

137. T. M. Barnes, Evaluation of Process Alternatives to Improve Control of Air Pollution from the Production of Coke, Batelle Memorial Institute, Columbus, Ohio, 1970.

138. Office of the Federal Register, General Service Administration, Office for Protection of Environment, App. B.

139. U.S. Environmental Protection Agency, Compilation of Air Pollutant Emission Factors (Second Edition), Publication No.

140. W. A. Daniel and J. M. Heuss, "Ambient Air Quality and Automotive Emission Control," Journal of the Air Pollution Control Association, Vol. 24 Number 9, September 1974.

141. Personal communication, B. Baratz, MITRE Corporation, December 1975.